Diagnostic Odyssey in ALS

Patient #3: Bulbar ALS with Frontotemporal Dementia

55-year-old-man

Case contributor and commentary:

Dr. Martina Wiedau, MD
University of California Medical Center | Los Angelas, California

Initial Symptoms

Medical History:

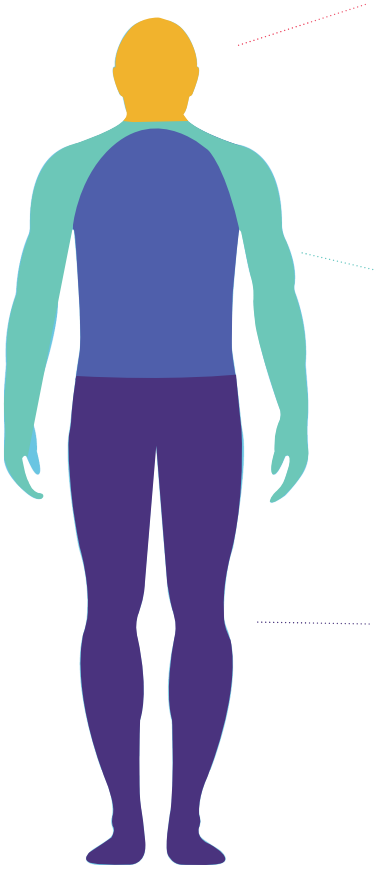
- Type 2 diabetes mellitus
- No family history of ALS or neurological disease

Family History:

- Early onset dementia in patient's father at age 61

Figure Key

- Bulbar region
- Cervical region
- Thoracic region
- Lumbar region
- Site of key/defining symptoms



- Altered behavior — more outgoing, increased appetite (2-3 months)
- Altered speech production, speaks haltingly in shorter sentences
- Fasciculations of tongue muscles and difficulty chewing, some slurred speech when tired (1 month)
- Right > left arm weakness, slowly processing (9 months)
- Reduced walking distance and leg stiffness (3 months)
- Noted muscle fasciculations and cramps in legs

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Physical Exam

Following observation of initial symptoms, a physical examination was performed:

- Mental status exam:
  1. normal alertness and orientation to self, time place and situation (A+O x4),
  2. normal attention, concentration,
  3. Memory: recall 3/3 at 5 minutes,
  4. Language: word generation list F-words: 7. Reduced comprehension, fluency naming, good repetition.
- Cranial nerves exam: lower facial weakness, tongue atrophy and fasciculations
- Motor exam: reduced bulk of FDI/first dorsal interosseus muscle, thenar, and interossei muscles right>left; increased tone B LE/lower extremities 3/4
- Weakness of FDI R 3/5, L 4/5, interossei R 1/5, R 2/5, B ADM 2/5
- Hip flexion R 5-/5, L 4+/5, + B leg fasciculations
- Deep tendon reflexes: 3+/4 B UEs/upper extremities, B ankle clonus and positive Babinski, snout reflex, jaw jerk
- Gait analyses: uses arms to stand up, slow spastic gait

Laboratory Tests

After the physical exam, follow-up tests were ordered:

Electromyography (EMG)/nerve conduction studies (NCS):

- Fibrillation, positive sharp waves and large polyphasic units of long duration firing at high rates with a reduced recruitment pattern
- The changes are widespread, including in clinically unaffected muscles
- Normal motor and sensory nerve conductions

Blood work :

- CK: 900, elevated
- Genetic testing: positive C9ORF72

Imaging:

- Moderate left temporal brain atrophy and normal C-spine MRI

Commentary: Familial ALS (fALS) accounts for 5-10% of all ALS cases.[1] Genetic testing can confirm a diagnosis of fALS and influence future clinical decisions. Historically, genetic testing was offered only to those who were suspected of having a family history indicating fALS, but increasingly it is recommended that all patients with ALS undergo a genetic test.

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Diagnosis

Differential Diagnosis:

The symptoms of progressive weakness of the left arm, dysarthria and dysphagia, leg spasticity with hyperreflexia and aphasia resulted in consideration of the following differential diagnoses:

- Cortical brain disorder
- Multifocal brain disorder

Criteria Used for Diagnosis:

- UMN features in bulbar, cervical and lumbar region
- LMN features determined by EMG in bulbar, cervical, and lumbar regions

Diagnosis:

Definite ALS per Airlie House and Awaji criteria

Disease Progression

The patient was diagnosed 13 months after his initial symptoms. The patient experienced the following course of disease, passing away from cachexia at 36 months after symptom onset:

Diagnosis at 13 months following symptom onset

Symptom onset	15 mos	20 mos	24 mos	32 mos	34 mos	36 mos
Progressive weakness of arms and legs						
	Started using walker					
		Cognitive deterioration with muteness				
			Developed bulbar symptoms			
				Significant weight loss, decided against PEG tube		
				Became unable to ambulate and bedridden		
					Passed away from cachexia	
						Passed away from respiratory failure

Commentary: ALS is part of a disease spectrum characterized by progressive muscle weakness, and often can be differentiated by widespread symptoms throughout the body vs a more localized or slower-moving progression seen in other disorders on the spectrum.

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ALS Disease Spectrum

Condition	Characteristics
Primary Lateral Sclerosis (PLS)	» Primarily UMN disease » Progressive » Slow course » Late LMN signs
Amyotrophic Lateral Sclerosis (ALS)	» UMN and LMN concomitant disease » Progressive » In multiple body regions
Progressive Bulbar Palsy	» Progressive weakness of bulbar muscles
Progressive Muscular Atrophy (PMA)	» Primarily LMN disease » Slower course
ALS and Frontotemporal dementia (FTD)	» Often linked to C9ORF72 mutations » 40% of familial ALS cases » 20% familial FTD cases

References

1. Siddique N, Siddique T. Amyotrophic Lateral Sclerosis Overview Synonym: Lou Gehrig Disease Goal 5 Provide a High-Level View of Management of ALS.; 1993.

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