Clinical characteristics of patients with bulbar onset ALS at an academic medical center.

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BACKGROUND

ALS is a neurodegenerative disease which results in progressive debility and death around 3-5 years from diagnosis. There are few pharmacologic interventions to modify disease course, and the medications used to treat ALS have only modest effects[1]. Non-pharmacologic treatments such as respiratory and nutritional support are extremely important in ALS. Studies show that early support with noninvasive ventilation can improve survival[2,3,4], and there is increasing attention to the importance of nutritional support for modifying the clinical course[5].

Patients with bulbar onset of ALS merit special attention from both clinical and research perspectives. They comprise about 25% of all ALS, and all patients with ALS will eventually develop bulbar dysfunction. Dysphagia early in the disease puts the patients at high risk of nutritional insufficiency, which is a poor prognostic factor[6,7]. Bulbar onset may also portend a higher likelihood of respiratory involvement, due to contiguous spread of motor neuron dysfunction and death to the cervical and thoracic spinal motor neurons. However, the diagnostic testing required in these patients (and the time taken from presentation to complete such testing) to exclude alternative pathologies may be less than that required for patients with limb onset symptoms, as there are fewer possible confounding comorbidities. Also, if the nutritional and respiratory needs of these patients (and patients with bulbar symptoms in general) are managed more effectively, we may be able to make a greater impact on their quality of life and survival.

Patients with bulbar onset ALS are an attractive population in which to study possible interventions, given that their limb strength at the time of symptom onset should be normal, and this would be a useful objective measure to track. Characterizing the clinical characteristics of our cohort would contribute meaningfully to the knowledgebase of the field, and may provide useful information for the formulation of future prospective trials in the population.

OBJECTIVES

Major objectives:

A) To characterize the clinical features of a cohort of bulbar onset ALS patients at the time of initial symptom presentation and over the course of their illness, and to compare some of these measures to those found in patients with limb onset ALS.

B) To examine how the timing and utilization enteral nutrition may affect the disease course in these bulbar-onset ALS patients.

Specific questions:

•Is there a difference from the time of symptom onset to the time of diagnosis for patients with bulbar vs limb onset in our cohort?

•In patients with bulbar onset ALS, is limb function typically normal at the time of suspected ALS diagnosis or have they already lost functional abilities?

•What is the time from initial symptom presentation to the spread of symptoms to a new body region? Does this typically occur before or after diagnosis of suspected ALS?

•What is the time frame over which limb weakness develops and progresses to end stage?

•Is early parenteral nutrition associated with changes in disease course?

METHODS

- A retrospective study reviewing the records of patients seen in the KNI ALS multidisciplinary clinic. Patients are first identified using the SlicerDicer tool in Epic, identifying a patient cohort that are in the UK ALS registry.
- We will examine the patient charts for the parameters of interest described below and create a REDCap database to compare the de-identified patient data.
- We will try to examine the data that was collected at many time points:
  - Prior to symptom onset, at time of symptom onset, at time of ALS diagnosis, and at each subsequent ALS clinic visit.

Data collection

- Demographic info: age, gender, ethnicity, race, occupation, prior military service.
- Baseline health parameters: height, premorbid weight, weight at diagnosis, other PMH including HTN, HLD, DM, CAD, COPD, obstructive or restrictive lung disease, prior head trauma or neurological surgeries. Family hx of dementia or ALS.
- ALS info: date of first symptom onset, first affected body region, initial symptoms, date of first symptoms in the second affected region and symptoms, date that ALS was first suspected, date of ALS diagnosis. ALS meds and start dates.
- Diagnostic workup: Other providers seen for the issue, various blood labs, lumbar puncture, brain imaging, ALS genetic testing, and EMG findings in the craniobulbar, cervical, thoracic, and lumbosacral regions.
- Parameters measured and tracked at each UK Neurology or ALS clinic visit:
  - Weight, BMI, absolute FVC and FVC% of predicted, status of BiPAP and PEG use, mobility status and wheelchair use/dependence.
  - Scores on the ALS Functional Rating Scale, and the time from symptom onset and/or diagnosis to the time of scores of 1 or 0 on the different subscales.

Table 1: The parameters evaluated by the ALS Functional Rating Scale-Revised (ALSFRS-R), divided by its 4 subcategories.
Scores of 0-4 are assigned for each function, 0 being the lowest **Bulbar:** Speech, salivation, swallowing **Fine motor:** Handwriting, Cutting food and handling utensils, Dressing and hygiene **Gross motor:** Turning in bed and Adjusting clothes, Walking, Climbing stairs **Respiratory:** Dyspnea, Orthopnea, Respiratory insufficiency

METHODS

Measures and Comparisons

Compare the time from first symptom onset to the time of diagnosis between patients with bulbar onset vs limb onset ALS.

Quantify the percentage of bulbar onset ALS patients having limb weakness or impaired limb function at time of diagnosis, and quantify their average scores on the ALSFR-R scale at time of diagnosis.

Will quantify the time from ALS diagnosis to the time of occurrence of the following major endpoints, and compare between bulbar and limb onset ALS patients:

1. A score of 1 or 0 score on the Gross or Fine motor subset of the ALSFRS score.
2. A score of 1 or 0 on the "Walking" score of the ALSFRS.
3. Wheelchair dependence.
4. A score of 0 on the "Speech" score of ALSFRS, ie anarthria.
5. Noted onset of depression, pseudobulbar affect.
6. Death.

We will look for possible correlations between earlier use of parenteral nutrition and changes in the time from symptom onset to the time of the above major endpoints.

RESULTS

Table 2: 291 total patients in the UK ALS registry were identified. A brief comparison of 26 patients in the ALS registry showed that 69% of these went on to have confirmed ALS diagnosis (with 31% having alternate diagnoses or lost to follow up), 28% of those had bulbar onset ALS and 72% had limb onset ALS.

	Percentage of examined patients	Total estimated patients
Estimated Confirmed ALS	69%	201
Estimated Limb onset ALS	19%	55
Estimated Bulbar Onset	50%	146

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