The Care of the Patient with Amyotrophic Lateral Sclerosis

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Overview:

- Clinical presentation, history, physical
- Evidence based review of available options for treatment
Diagnostic Triad: ALS

Upper motor neuron

Progression

Lower motor neuron
Motor Neuron Disease: Diagnostic Dilemmas
ALS Demographics

- Incidence 2 per 100,000
- Female slightly > male
- Peak age of onset: 6th decade, range <20 to >90
- No racial predilection
- 95% sporadic
- 5% AD (FALS)*
ALS: Pathology
ALS Diagnosis: Upper Motor Neuron Symptoms

- Loss of dexterity
- Slowed movements
- Loss of muscle strength in UMN pattern
- Stiffness/spasticity
- Emotional lability
  - Aka Pseudobulbar affect
ALS Diagnosis: Upper Motor Neuron Signs

**Upper Extrem**
- UMN weakness
- Pathologic DTRs
- Hoffman’s
- Spasticity

**Bulbar**
- Jaw jerk
- Palmomental reflex
- Glabellar blink
- Dysphagia
- Dysarthria

**Lower Extrem**
- UMN weakness
- Pathologic DTRs
- Babinski reflex *
- Rossilomo reflex

**Thoracic**
- Incr Abd reflexes
ALS Diagnosis: Lower Motor Neuron Symptoms/Signs

- Loss of muscle strength
- Atrophy
- Fasciculations
- Muscle cramps
- Dyspnea, dysphagia, dysarthria
ALS DIAGNOSIS

Clinical Picture

Signs and symptoms at initial presentation

- 63.2% Weakness
- 22.0% Bulbar signs
- 9.7% Atrophy
- 8.8% Pain and cramps
- 3.5% Fasciculation
- 3.5% Paresthesia
- 2.2% Weight Loss
- 1.3% Spasticity
- 0% Hypotonia
- 4.1% Data not recorded

Percentage of 318 patients in an Israeli study presenting with symptom (1959-1975)

ALS DIAGNOSIS

Location of Weakness at Presentation Frequency

- 63.2% Weakness
- 19.8% Paraparesis
- 11.9% One leg
- 10.7% One arm
- 8.5% Both arms
- 8.5% Generalized
- 3.8% Hemiparesis

Percentage of 318 patients in an Israeli study presenting with symptom (1959-1975)

ALS: Inconsistent Clinical Features

- Sensory dysfunction (unless other PN)
- Bladder and bowel sphincter dysfunction* (SCA)
- Autonomic nervous system dysfunction
- Movement disorders
- Cognitive abnormalities other than frontotemporal dementia (this is found in up to 50%)
ALS: Differential Diagnosis

- Cervical spondylosis
- Diabetic polyneuropathy (esp. if + another UMN etiology such as CVA/cervical stenosis/etc)
- Spinocerebellar ataxia
- Genetic spastic paraparesis
- Kennedy’s disease (SBMA)
- Spinomuscular atrophy (SMA)
- Metabolic (hyperthyroidism, hyperparathyroidism, hypoglycemia)
- Enzyme deficiency (Hexosaminidase A)
- Paraneoplastic (lymphoma, small cell lung)
ALS: Differential Diagnosis

- Immunologic (paraproteinemia)
- Multi-system degeneration (Creutzfeldt-Jacob, ALS-PD-Dementia)
- Viral (Post-polio, Enterovirus)
- Bacterial (Lyme disease)
- Vitamin B12 deficiency
ALS: Work-up

Usual
- SMA-12
- CK
- SPEP
- B12
- TSH, (PTH)
- EMG/NCV*
- MRI Cerv/Brain/Etc
- EXAM

Possible based on history and exam:
- Lyme titer
- HIV
- Hexos A level
- LP
- Muscle biopsy
- Genetic testing for SBMA/SCA/HSP
ALS: Laboratory Studies

- CK levels are typically normal but may be increased 2-3x normal in almost half of patients.*

- CSF may show mild protein elevation (less than 100mg/dl).*

- All other laboratory studies should be normal, unless explained by concurrent disease
ALS: El Escorial Diagnostic Criteria

- Signs of LMN degeneration by clinical, electrophysiologic, or neuropathological examination and

- Signs of UMN degeneration by clinical examination and

- Progressive spread of signs within a region or to other regions and

- Negative laboratory (except CK) and neuroimaging studies.
ALS: Prognosis

- Rochester, MN (3/5/10 year survival rates)
  - 50% dead in 3 years
  - 20% live 5 years
  - 10% live 10 years

- Worse prognosis if:
  - Bulbar onset
  - FALS
  - Simultaneous arm/leg onset
  - Older age at diagnosis (onset < 40: 8.2 yr duration, onset 61-70: 2.6 yr duration)
CARE OF THE ALS PATIENT

A Team Approach

Physician(s)

Patient support groups

Nurse

Social worker

Respiratory therapist

Pharmacist

Speech-language therapist

Dietician

Mental health specialist

Family/primary caregivers

Physical therapist

Occupational therapist

Patient
Treatment Issues to Consider

- Symptom management
- Nutritional management
- Respiratory management
- Therapies to slow disease progression
- Caregiver support
- Palliative care
Symptoms Associated with Motor Neuron Disease

- Dysarthria
- Dysphagia
- Sialorrhea
- Emotional lability
- Depression
- Weight Loss
- Bladder urgency
- Sleep dysfunction
- Constipation
- Edema
- Pain
- Spasticity
- Cramps
- Fatigue
- Weakness
ALS Practice—What works?

- AAN Practice Parameters October 2009
- The care of the patient with amyotrophic lateral sclerosis
  - Drug, Nutritional, and Respiratory Therapies
- Multidisciplinary Care, Sx Management, Cognitive/Behavioral impairment
Evidence Classes I to IV

- **Class I:** Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population.
  - The following are required:
    - a) primary outcome(s) is/are clearly defined
    - b) exclusion/inclusion criteria are clearly defined
    - c) adequate accounting for drop-outs and cross-overs with numbers sufficiently low to have minimal potential for bias
    - d) relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

- **Class II:** Prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR a RCT in a representative population that lacks one criteria a-d.

- **Class III:** All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment.

- **Class IV:** Evidence from uncontrolled studies, case series, case reports, or expert opinion.
Multidisciplinary ALS Clinics

- Evidence for Multidisciplinary Clinics
  - Increase use of riluzole, PEG, NPPV in ALS clinics and fewer unplanned hosp admits (Class II)
  - Prolonged survival by 7.5 months (Class II)
  - Independent predictor of survival and reduced death risk by 47% (Class II)
  - Received more aids and appliances, higher QOL scores (Class III)
RILUTEK® (riluzole) Tablets

Higher Tracheostomy-free Survival Rates after 12 and 18 Months

Study 1
- 12-Month Survival: 74%
- 18-Month Survival: 49%
- n=155

Study 2
- 12-Month Survival: 74%
- 18-Month Survival: 57%
- n=959

- Approximate increase in median survival
  - Study 1: 3 months during the 13 to 18 months of Rilutek therapy
  - Study 2: 2 months during the 12 to 18 months of Rilutek therapy
Riluzole

- Prolongs life by 2-3 months (Class I)
- Maybe as long as 6 months (Class II)
- Maybe as long as 21 months (Class III)

Dosing
- 50mg qhs for 2 weeks, then 50 mg bid
- 14% cannot tolerate-asthenia/nausea most common SE
- Antiglutamergic agent

MONITOR
- Serum ALT levels should be evaluated every month during the first 3 months of treatment,
- Every 3 months during the remainder of the first year, and
- Periodically thereafter. Serum ALT levels should be evaluated more frequently in patients who develop elevations.
Sialorrhea-seen in 50% of pts

- Symptoms result from inability to clear oropharyngeal secretions
- Pharmacologic treatments (effective in 70% of pts):
  - Glycopyrrolate (Robinul) 1-2 mg q 4h
  - Amitriptyline (Elavil) 25-100 mg qhs
  - Hyoscyamine sulfate (Levsin) 1-2 tsp q 4h
  - Transdermal scopolamine
  - Botulinum toxin into parotids and/or submandibulars (Class I)
- Suction machines, In-exsufflator
- Radiation tx (Class III)
Management of Emotional Lability

- Common nonpharmacologic treatments:
  - Counseling/support groups
  - Establishment of a daily routine
  - Management of other symptoms

- Common pharmacologic treatments:
  - Amitriptyline (Elavil) 25-150 mg qhs*
  - SSRIs
  - Dextromethorphan/quinidine 30mg bid-24% cannot tolerate (Class I)
No evidence-based recommendations

- Fatigue
- Cramps
- Spasticity
- Depression
- Anxiety
- Insomnia
- Cognition-(possible screening tests)
- Palliative care
- Withdrawal of ventilation
Spasticity

- **Common pharmacologic treatments***:
  - Baclofen (Lioresal) 10-40 mg TID-QID
  - Dantrolene sodium (Dantrium) 25 mg qd - QID
  - Tizanidine HCL (Zanaflex) 12-36 mg TID
  - Diazepam (Valium) 2-5mg TID
  - Baclofen pump

- **Common nonpharmacologic treatments**:
  - Physical therapy
  - Slow (30 sec sustained) static muscle stretching
Management of Dysphagia: Indications for PEG

- Significant weight loss
- Inadequate fluid (2-3 liters) or caloric intake
- Difficulty swallowing medications
- Frequent choking during meals
- Prolonged meal times
- FVC < 50%
- Aspiration pneumonia
Enteral nutrition (PEG)

- Stabilizes weight (Class II)
- Risks of PEG-laryngeal spasm, local infection, gastric hemorrhage, death due to resp arrest
- Less risk if placed when FVC > 50% of predicted (Class III)
- Unclear if PEG users have prolonged survival
- PEG does not contraindicate oral feeding
  - Reduces fatigue due to prolonged feeding times
Nutritional Management Algorithm

Diagnosis: ALS

- Clinic visits every 3 months
  - Early dysphagia detected
    - Nutritional education including PEG
      - Nutritionist or speech therapist referral
    - Monitor Respiratory status (FVC, MIP, etc.)
      - Clinic visits every 3 months
        - Symptom progression or continuing weight loss
          - Discuss PEG to stabilize weight and possibly prolong survival

- FVC >50%
  - Low risk for PEG
    - PEG accepted

- FVC 30-50%
  - Moderate risk
    - Anesthesia evaluation
      - Experienced gastroenterologist
        - Respiratory support during PEG if needed
      - Oral intake as tolerated
        - Enteral nutrition via PEG as needed
    - PEG accepted

- FVC <30%
  - High risk
    - PEG declined
      - Oral intake as tolerated
        - Palliative IV hydration
          - Palliative NG feeding
Respiratory Management

- Respiratory failure due to weakness usual cause of death in ALS pt
  - Not painful, CO2 retention → narcosis effect → CV arrhythmia

- How to measure respiratory status? (*indications for NPPV)
  - % predicted FVC most common (< 50% pred FVC)
  - MIP/MEP mean inspir/expir pressures (< 60 cm)
  - Nocturnal desats (<90% for > 1 minute)
  - Nocturnal oximetry (mean O2 sats < 93%)
  - Sniff nasal pressure SNP (< 40 cm)
  - Cough pressures impt to clear secretions-want peak cough expiratory flow > 270 L/min
Respiratory Insufficiency:
Early Symptoms-must ask pts at visit

- Dyspnea on exertion
- Supine dyspnea
- Marked fatigue
- Excessive daytime somnolence
- Frequent nocturnal arousals
- Vivid dreams
- Morning headaches
Effect of NPPV on Survival in ALS Patients

- FVC declined more slowly after introducing NIV (pre –2.2%/mo vs. post –1.1%). (class I and III)
- the decline was slower in those who used NIV > 4 hours/day. (class III).
Effect of NPPV on Survival in ALS Patients

- Compared survival and FVC% decline between tolerant (n=23) and intolerant patients (n=24).
- Median survival in intolerant patients was 5 months compared to 20 months in tolerant patients (p=0.002).

Effect of NPPV on Survival in ALS Patients

- ALS patients using NPPV had a median survival benefit of 205 days-! (Class I)

Management of Respiratory Muscle Weakness

- Consider initiation of NPPV when:
  - Symptoms of nocturnal hypoventilation
  - FVC <50% of predicted
  - MIP < -60 cm H2O
  - Evidence of significant O2 desaturations on nocturnal oximetry studies
Respiratory Management Algorithm

Text in bold = evidence-based
Text in italics = consensus-based

Diagnosis ALS

Symptom evaluation* and PFTs
Initiate NIV orientation,
Pneumovax and flu vaccine

Orthopnea or
SNP < 40cm or MIP < -60cm
or Abnl nocturnal oximetry or
FVC < 50%

Consider NIV

NIV tolerated?

No

Further education regarding documented benefits.
Evaluate reasons for noncompliance.

Yes

Reintroduce NIV

Successful

Unable to maintain pO₂ > 90%, pCO₂ < 50mmHg or unable to manage secretions

Not successful

Hospice referral for palliative care

Invasive ventilation

Ongoing evaluations and adjustment of pressures

PCEF < 270 L/min

Suction machine
Manual assisted cough
Mechanical inexcusificator
Treat sialorrhea/phlegm
Management of Weakness: Assistive Devices

- Assistive communication
- Cane
- Roll-aided walker
- AFOs
- Wheelchair
- Hoyer lift
- Cervical collar
- Hospital bed
- Ramps

- Built-up utensils
- Velcro fasteners
- Raised toilet seat
- Shower chair
- Resting hand splints
- Grab bars
Palliative Care

- Treatment of terminal dyspnea:
  - Roxanol 5-30 mg q 4h
  - Oxygen (1-2 liters)
  - Lorazepam 0.5 - 2 mg SL
  - Chlorpromazine 25 mg PR q 4-12h

- Educate patient, family, and hospice that all of the above measures may depress the respiratory drive.
ALS and Veterans Affairs

9/22/03- study found that veterans who were deployed to the combat theater during the Gulf War were nearly twice as likely to develop the disease as veterans not deployed to the Gulf, accounting for 40 of the 107 cases identified among military personnel. The incidence of ALS was especially high among deployed Air Force personnel, who were 2.7 times more likely to develop ALS than non-deployed Air Force personnel.
WASHINGTON – Veterans with amyotrophic lateral sclerosis (ALS) may receive badly-needed support for themselves and their families after the Department of Veterans Affairs (VA) announced today that ALS will become a presumptively compensable illness for all veterans with 90 days or more of continuously active service in the military. “Veterans are developing ALS in rates higher than the general population, and it was appropriate to take action,” Secretary of Veterans Affairs Dr. James B. Peake said.
VA Medical Care for ALS
How we might be better than the private care

- Multidisciplinary care organization already intact (SCI)

- Constrictions of private care not present or as pronounced
  - ALS pts could come for monthly visits as needed (vs q3mo)
  - ALS pts can be admitted to SCI for convenience, multidisciplinary approach, and efficiency of care
  - Assistive technology such as WC much quicker in VA
  - Restrictions on providing NPPV not present at VA—the most effective therapy
What needs to be done here at the VA

- Establish multidisciplinary ALS clinic at VA-? q month
  - Identify who is interested and can be involved

- Incorporate ALS patient non-profit: ALS Association
  - Steve Elkin MSW ph 781-255-8884, ext 243

- Consider establishing ALS resource center to support high level ALS care at distant VAMCs and OPCs who may have fewer pts
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