1 □ DIFFERENTIAL DIAGNOSIS OF PROGRESSIVE LANGUAGE DISORDERS

2 □ DISCLOSURES
  • A portion of my salary is covered by the NIH to study patients with PPA and PPAOS.
  • I receive royalties for a book published with Plural Publishing.
  • I have no other financial or non-financial disclosures.

3 □

4 □ LEARNING OBJECTIVE
Learners will:
  • describe the clinical diagnostic inclusion and exclusion criteria for the three primary variants of primary progressive aphasia (PPA).
  • summarize the neuroimaging findings associated with each variant of PPA.
  • outline the tasks that are useful in the differential diagnosis of PPA variants.

5 □ OUTLINE FOR TODAY’S TALK
  1. What is PPA?
     • What is not PPA?
  2. Approach to differential diagnosis
  3. Management Overview
     1. Counseling
     2. Intervention
  4. Case Studies

6 □ PLEASE, NO VIDEOS OR PHOTOS OF PATIENTS

7 □ WHAT IS PRIMARY PROGRESSIVE APHASIA?

8 □ PRIMARY PROGRESSIVE APHASIA
  • A spectrum of degenerative disorders characterized by initial language problems
  • A clinical syndrome
    • not a single underlying pathology
  • Does not include patients in whom aphasia is just a manifestation of dementia

9 □ PPA ROOT CRITERIA
  • Insidious and progressive course
  • Language dysfunction is the initial feature
  • Impairments in activities of daily living stem primarily from language difficulty
  • Language remains the most prominent deficit in the early phase of the disease
  • The following are not present
    • Early, prominent behavioral changes
    • Early, prominent memory disturbance
    • Early, prominent motor disturbance

10 □ GORNO-TEMPINI ET AL. DIAGNOSTIC CRITERIA
  • Logopenic variant
  • Semantic variant
• Agrammatic/ Non-fluent variant

11 □ LANGUAGE AREAS
• Phonology
• Morphology
• Syntax
• Semantics
• Pragmatics

• All areas may be impacted, particularly later in the disease course, but looking for area of disproportionate impairment

12 □ LOGOPENIC PPA
• Both:
  • Impaired single-word retrieval
  • Impaired repetition of sentences
• At least 3:
  • Phonological errors
  • Spared single-word comprehension and object knowledge
  • Spared motor speech
  • Absence of agrammatism

13 □ LOGOPENIC VARIANT OF PPA
• A slow rate of verbal expression, secondary to word retrieval difficulties
• Phonologic errors may be present
• Reading and writing abilities may be preserved longer than speech

14 □ HOW DO THESE PATIENTS LOOK AND SOUND?

15 □ LOGOPENIC PPA
• Typically associated with Alzheimer’s pathology

16 □ EVOLUTION OF DISEASE
• Evolving neurologic picture
  • No specific pattern of motor impairment
  • Reduced inertia and interactions
• Neuropsychological/ neuropsychiatric changes
  • May develop other features of Alzheimer’s disease
    • Prominent memory issues
    • Calculation
    • Visuospatial skills
    • Attention
    • Executive function

17 □ SEMANTIC PPA
• Both
  • Impaired confrontation naming
  • Impaired single-word comprehension
• At least 3:
  • Impaired object knowledge
  • Surface dyslexia or dysgraphia
  • Spared repetition
  • Spared speech production (grammar and motor speech)

18  □  SEMANTIC VARIANT OF PPA
  • Anomia with loss of single word meaning
    • Comprehension
    • Confrontation naming
      • Rare words affected first; common nouns later; verbs and abstract words are often spared
  • Surface dyslexia or dysgraphia
  • Fluent spontaneous speech is mostly retained
  • Prosopagnosia/ object agnosia

19  □  SEMANTIC PPA
  • May have significant behavioral problems during disease progression
    • Patients obsessed with puzzles
    • Cold and emotionless
    • Food fads
  • Least likely to be associated with parkinsonism, motor neuron disease and to be familial

20  □  HOW DO THESE PATIENTS LOOK AND SOUND?

21  □  PICTURE DESCRIPTION

22  □  SLB NAMING (SCORED 4/16)

23  □  SLB SEMANTIC ASSOCIATION (SCORED 19/30)

24  □  WRITTEN PICTURE DESCRIPTION

25  □  SEMANTIC VARIANT OF PPA
  • Report difficulty with writing and spelling, particularly with irregularly spelled words
  • Surface dyslexia

26  □  IRREGULAR WORDS

27  □  NONWORDS

28  □  SURFACE ALEXIA

29  □  SEMANTIC PPA
  • Typically associated with TDP-43 pathology

30  □  “SEMANTIC DEMENTIA”

31  □  EVOLUTION OF DISEASE
  • Tends to become bilateral
    • Converges on language-behavioral problems
  • Changes in:
    • Disinhibition
• Personality (compulsions, obsessions)
• Social cognition
• Memory
• Executive function
• Evolving neurologic picture
  • Motor functioning typically preserved

32 □ AGRAMMATIC/ NON-FLUENT VARIANT OF PPA
• At least 1
  • Agrammatic or telegraphic output
  • Apraxia of speech (AOS)
• At least 2
  • Reduced comprehension for grammatically complex sentences
  • Spared single-word comprehension
  • Spared object knowledge

33 □ AGRAMMATIC PPA
• Problems with grammar (agrammatism):
  • “Are to store you going”
• Brief, ‘telegraphic’, omission of smaller words
  • “fly home soon”
• Reversals (e.g., “yes” for “no”; “thank you” for “you’re welcome”)

34 □ SYMPTOMS OF AGRAMMATISM

35 □ HOW DO THESE PATIENTS LOOK AND SOUND?

36 □ PICTURE DESCRIPTION

37 □ WRITTEN PICTURE DESCRIPTION

38 □ WRITTEN PICTURE DESCRIPTION

39 □ AGRAMMATIC PPA
• Typically associated with tau pathology

40 □ EVOLUTION OF DISEASE
• Evolving neurologic picture
  • May progress to atypical parkinsonism [corticobasal syndrome (CBS) or progressive supranuclear palsy (PSP)] or bvFTD
  • Motoring slowing/ limb apraxia
  • Gaze palsy
• Neuropsychological/ neuropsychiatric changes
  • Working memory
  • Planning
  • Apathy, depression, and/or irritability
  • Disinhibition

41 □
• Patients with isolated agrammatic aphasia
• performed better on tests of motor speech and parkinsonism but more poorly, and declined faster over time, on tests of general aphasia severity, agrammatism, and naming
  • compared to the patients with mixed AOS and aphasia

42 □ UNCLASSIFIABLE PPA
  • Many patients who meet root criteria for PPA are not clearly classifiable into one of these variants, making diagnosis particularly challenging

43 □ UNCLASSIFIABLE PPA
  • The current diagnostic criteria fall short of capturing all cases of PPA (12-30% of patients!)
  • Data driven PCA
  • 3 PPA variants are represented in this cohort of unclassifiable patients, both in clinical and imaging profiles

44 □ WHAT IS NOT PPA?
  • PPA implies a language problem.
  • In the nonfluent/agrammatic variant, patients can have AOS in the absence of aphasia.

46 □ Primary Progressive Aphasia of Speech

47 □ PPAOS

48 □ PPAOS DIAGNOSTIC CRITERIA

49 □ PATIENT PERCEPTIONS AND COMPLAINTS
  • “my speech won’t come out right”
  • “I know what I want to say but I can’t get it out”
  • “I mispronounce words”
  • “I have to pause to continue”
  • “I can’t speak as quickly”
  • “I have to speak more carefully to prevent errors”
  • Patients predict errors on multi-syllabic or difficult to pronounce words
  • They recognize errors and attempt to correct them

50 □

51 □ HOW DO THESE PATIENTS LOOK AND SOUND?

52 □ BUT ALSO LIKE THIS

53 □ MOTOR PROCESSES OF SPEECH

54 □ PPAOS TYPES

55 □ CLASSIFICATION IS NOT DICHOTOMOUS, BUT A RELATIVE PREDOMINANCE

n = 42  n = 35

57 □

• Approximately 80% of patients with PAOS were imprecisely diagnosed at their first visit
• median of 3 years from symptom onset to receiving PAOS diagnosis
• Being seen by a speech-language pathologist during the initial evaluation increased the likelihood of a correct diagnosis.

DEMOGRAPHICS

• Also typically associated with tau pathology
• May progress to atypical parkinsonism

IMAGING: FDG
• Hypometabolism on fludeoxyglucose positron emission tomography (FDG-PET) typically occurs in same areas
• Abnormalities may be more noticeable on the individual level compared to MRI

CONTINUUM

EVOLUTION OF DISEASE
• Similar to that of nonfluent/agrammatic PPA
  • BUT we know the clinical trajectories are different

EVOLUTION
• All patients develop:
  • parkinsonism
  • worsening of their apraxia of speech
• Many patients develop:
  • Motoring slowing/limb apraxia (Phonetic)
  • Gaze palsy (Prosodic)
• Phonetic: faster rates of decline in motor speech and aphasia
• Prosodic: poorer scores on the UPDRS; onset of aphasia may be later
• Neurologic syndromes:
  • Corticobasal syndrome
  • Progressive supranuclear palsy

EVOLVING SPEECH-LANGUAGE PICTURE
• Dysarthria
  • Evident in <30% of pts at 2-4 years post onset
  • Most commonly spastic, hypokinetic, or mixed spastic-hypokinetic
• Dysphagia is common, but typically not until after dysarthria emerges
• Aphasia
  • Emerges in 40-50% of patients by about 5 years post symptom onset
  • Prevalence increases after 5 years but onset can be delayed until 10+ years
• AOS remains the most prominent symptom
• Cross-sectionally
  • Prosodic AOS produced words more slowly than those with phonetic AOS.
  • Patients with either aphasia or dysarthria produced words more slowly than those without
• Longitudinally
  • Speech rate of patients with phonetic AOS reduced 0.5 syllables per second per year.
  • Patients with prosodic AOS changed less quickly.

SURVIVAL
• Estimated survival ~ 9 years post-symptom onset for PPAOS (longest; 6 years from baseline visit)
• Estimated survival ~ 7-8 years post-symptom onset for AOS+PAA (4 years from baseline visit) and
  PAA (5 years from baseline visit)

NEUROPATHOLOGY
• CBD pathology is the most common
  • Followed by PSP
• Phonetic subtype and younger age predicted CBD
• Prosodic subtype and older age predicted PSP

APHASIA IN THE CONTEXT OF OTHER NEURODEGENERATIVE DISEASE
THE LANGUAGE PROBLEMS OF DEMENTIA
• Language is a cognitive function!
• But also: not all disruptions in verbal communication are aphasia
  Examples
  • Creutzfeldt-Jacob Disease (CJD)
  • Alzheimer’s disease dementia
  • Parkinson’s disease dementia
  • Lewy body dementia
  • Multiple Systems Atrophy
  • Behavioral variant FTD

AN EXAMPLE
• 2-year history of progressive word-finding difficulties
• “Forgets words” and other things
• Sent to me with a question of aphasia- was this PPA?

VIDEO
• Is this aphasia?
• What does he have?