CHAPTER
19

Slowly Progressive Aphasia

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Several cases of slowly progressive aphasia without dementia have been reported in the literature (Chawluk et al., 1986; Duffy, 1987; Heath, Kennedy, and Kapur, 1983; Horner, 1985; Kirschner, Tanridag, Thurman, and Whetsell, 1987; Mesulam, 1982), but there remain unanswered questions about this syndrome. It remains to be seen whether this syndrome develops into a dementia of the Alzheimer type (Foster and Chase, 1983; Kirschner, Webb, Kelly, and Wells, 1984; Mesulam, 1987; Neils and Barrett, 1987; Pogacar and Williams, 1984), and we have yet to determine the underlying neuropathology of this syndrome (Chawluk et al., 1986; Kirschner et al., 1987; Morris, Cole, Banker, and Wright, 1984). Additionally, we still do not know much about the development (rate of progression) or the epidemiology of this disease.

This chapter presents three cases of slowly progressive aphasia. In addition to case histories, we will present language, memory, computed tomography (CT), and positron emission tomography (PET) data.

METHOD

LANGUAGE AND MEMORY

The patients were tested with the full Western Aphasia Battery (WAB) (Kertesz, 1980) and, on a separate day, with a set of neuropsychological tests (Riege, Harker, and Metter, 1986) that tap attention, problem solving, and verbal and nonverbal memory and generally discriminate left- from right-hemisphere functions. The tests included the Raven's Coloured Progressive Matrices (Raven, 1956), the WAIS-R Block Design (Wechsler, 1955, 1981), the Visual Sequential Memory subtest of the ITPA (Kirk, McCarthy, and Kirk, 1969), the Seashore rhythm test (Seashore, Lewis, and Saetveit, 1960), and tests of information processing specific to verbal (words), visual (designs), and auditory (bird calls) modalities (Riege, Metter, and Hanson, 1980).

NEUROIMAGING

To ascertain neurofunctional information, patients were studied with fluorodeoxyglucose (FDG) PET in a resting state with eyes and ears unoccluded. The cerebral metabolic rates of 15 brain regions from each hemisphere were calculated for each patient as well as for 22 healthy age-matched controls.

Each patient also underwent noncontrast CT scan with scanning in the same plane as PET. The same regions as measured for glucose metabolism
were rated on a five-point scale (0 = normal, 1 = atrophy, 2 = structural damage with no tissue loss, 3 = structural damage with partial tissue loss, 4 = structural damage with complete tissue loss) by a neuroradiologist who was naive to the project and by one of the authors. The three cases are presented individually below.

CASE 1

History

E.G. is a 56-year-old left-handed male with a history of difficulty remembering words, names, and faces that has progressed very slowly over the past 15 years. He has been a puzzle to nearly all doctors he has seen and has an impressive list of diagnoses, including chronic endogenous or possibly psychotic depression, sarcoid brain lesion, slow-growing glioma, toxin exposure, Alzheimer's disease, hippocampal damage, and Pick's disease. Medical records over a 15-year period document the progressive decline of function. E.G.'s early educational and occupational functioning were superior. He holds a BA degree from Dartmouth, an MBA degree from Columbia and enjoyed a successful sales career with IBM Corporation. He first noticed word-finding problems in the early 1970s. The problems progressed until they interfered with his ability to work in 1977-78. At that point, he was laid off. Since then his ability to find and understand words and recognize faces has consistently deteriorated. He now participates in the compensated work therapy program at a VA Medical Center, where he performs unskilled labor.

Test Data

Word-finding continues to be E.G.'s most pronounced deficit. He was unable to name any of 20 objects presented on the WAB. Comprehension was mildly impaired. Repetition appeared relatively preserved. Reading for comprehension was severely impaired, but writing was appropriate and legible. He performed within normal limits for his age on Raven's Progressive Matrices, demonstrating a relatively strong island of nonverbal intelligence. Nonverbal memory including immediate and delayed memory for nonverbal stimuli (bird calls) was average. He demonstrated particularly poor performance on recognition of famous faces and all verbal memory tests (e.g., sentence and story recall). Three-dimensional drawing and the ability to perform simple calculations were intact.

Brain Structure and Function

A CT scan documented slightly generalized atrophy, with slightly enlarged ventricles, and sulci. A PET scan documented significant hypometabolism in the left temporal and parietal areas.
CASE 2

History

V.A. is a 71-year-old right-handed male with a 3-year history of rapid decline in word-finding and other speech production abilities. V.A. had been employed as a farmer, a dry-food packer, and in real estate. The patient failed to pass a test for a broker's license in early 1984, which prompted the initial concern, and soon after he was forced to retire due to his deteriorating condition. His major complaints center around communication: his voice is too low, he has difficulty speaking quickly, and he often has trouble getting words out. He also complained of stuttering, decreasing memory, and trouble with handwriting.

Initially, V.A. was diagnosed with "slow dysprosodic hypophonic verbal output with stutter." The presence of a somewhat shuffling gait, mild rigidity of the extremities, and a general slowness was consistent with a diagnosis of Parkinson's disease. However, the stuttering behavior was atypical of Parkinson's.

Subsequent evaluations by two neurologists and a neurolaryngologist revealed similar findings, all mentioning the diagnosis of Parkinson's disease and simultaneously noting the atypical presentation. Treatment with dopaminergic drugs had no notable effect on the symptoms. Neither a resting tremor nor festination were observed. Tongue movement was relatively rapid compared to other patients with basal ganglia disease. Although speech production (low volume, harsh breathy voice quality, monotone) was consistent with extrapyramidal disease and typically parkinsonian, the presentation of severe speech disturbance, with only mild (or inconsistent) other parkinsonian symptoms, has led to some questioning of the diagnosis.

Test Data

Language and memory evaluation were completed approximately 3 years after V.A. first noticed speech and language symptoms. His language symptoms were mild to moderate, with particular deficits in repetition, and difficulty understanding sentences (sequential commands 67 percent correct). Confrontation naming (95 percent correct) gives a possibly false impression of preserved word-finding and fluency; in conversation, he is often unable to generate sentences at all and demonstrated many apparent word-finding difficulties.

Nonverbal intelligence and perception (Ravens, Block Design, and Pattern Reconstruction) were within normal limits. Nonverbal memory (for designs and bird calls) was good. Verbal memory for printed words was also good. Deficits appeared severe where verbal output was required (e.g., verbal recall). He also performed below age norms on famous face recognition.

Brain Structure and Function

A CT scan showed mild generalized atrophy, and a PET scan showed marked focal hypometabolism in the left frontal, superior temporal, inferior
parietal, and thalamic regions, as well as the insula and head of caudate. Relatively spared regions included inferior and middle temporal, superior parietal, occipital, cingulate body of the caudate, and cerebellum.

CASE 3

History

R.S. is a 63-year-old right-handed male with a history of word-finding difficulties that has developed over the past 5 years. Prior to this time, the patient was a high-functioning engineer. Initial diagnosis included a workup for brain tumor, but all confirming tests were negative. The patient's complaints centered around anomia or, in his words "the dropping of the words. It is losing it, and uh, I like great, great, and so forth."

Test Data

Language and memory testing took place approximately 5 years after anomia was first noticed. Verbal output was fluent, but paraphasic in all tasks, including repetition and naming. Comprehension was relatively preserved, with some deficit noted in understanding sequential commands. Writing contained paraphasic errors, similar to those noted in speech production. Nonverbal intelligence (Raven's Matrices) appeared good as did auditory memory for nonverbal stimuli (bird calls). Calculation, visual sequential memory, and perception of rhythm all appeared impaired.

Brain Structure and Function

CT scans over the past few years have been uniformly negative. The most recent CT scan did reveal mild to moderate generalized atrophy, greatest in the left perisylvian area. The PET scan demonstrated left temporal hypofunction, which appeared to extend to the left frontal areas and thalamus.

SUMMARY AND DISCUSSION

The three cases differ from one another clinically. One case presented with a slowly (15 years) progressing memory problem that affected verbal and visual information; another case presented with a more rapidly progressing (over 3 years) disorder that included hypokinetic dysarthria and anomia; and the third case presented with a more slowly progressing (5 years) anomia with some other symptoms of left-hemisphere functions, including a calculation deficit, and poor perception of rhythm. The major behavioral and neuroimaging findings are summarized in Table 19-1. The remainder of this discussion will integrate these data into existing controversies about the nature of the progressive aphasia syndrome.
### TABLE 19-1. SUMMARY OF BEHAVIORAL AND NEUROIMAGING DATA

<table>
<thead>
<tr>
<th>Age at onset</th>
<th>Years since onset</th>
<th>Language characteristics</th>
<th>Non-language symptoms</th>
<th>CT findings</th>
<th>PET findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>41</td>
<td>15+</td>
<td>Naming (17%)</td>
<td>Visual memory</td>
<td>Bilateral atrophy</td>
<td>Left temporal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Comprehension (71%)</td>
<td>Face recognition</td>
<td></td>
<td>Left parietal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Repetition (92%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>68</td>
<td>3</td>
<td>Repetition (71%)</td>
<td>Dysarthria</td>
<td>Bilateral atrophy</td>
<td>Left temporal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Comprehension (86%)</td>
<td></td>
<td></td>
<td>Left parietal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Naming (90%)</td>
<td></td>
<td></td>
<td>Left frontal</td>
</tr>
<tr>
<td>58</td>
<td>5+</td>
<td>Repetition (45%)</td>
<td>Calculation</td>
<td>Bilateral atrophy</td>
<td>Left temporal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Naming (61%)</td>
<td>Visual sequence memory</td>
<td></td>
<td>Left frontal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Comprehension (90%)</td>
<td>Rhythm</td>
<td></td>
<td>Left thalamus</td>
</tr>
</tbody>
</table>
It has been suggested that cases such as those described are early presentations of a generalized dementia, possibly of the Alzheimer type (Foster and Chase, 1983; Gordon and Selnes, 1984; Kirschner et al., 1984). The symptoms in these individuals have developed over 3, 5, and 15 years since initially being reported. Although each case has deficits beyond strictly language symptoms, none of the cases yet, after several years, satisfies current diagnostic criteria for Alzheimer's disease by demonstrating cognitive deficits in several (i.e., three) major areas of cognitive function. Also, uncharacteristically of dementia, all three demonstrated relatively normal levels of nonverbal problem-solving ability (Raven's Progressive Matrices). These three cases, then, support those investigators who have claimed that there is a syndrome of progressive language impairment without generalized dementia (Heath, Kennedy, and Kapur, 1983; Kirschner et al., 1987; Mesulam, 1987).

These three cases add to our growing knowledge of the time course and epidemiology of the disease. Although we have documented impairments at only one point in time, from past medical records, it is clear that this syndrome is progressive. However, even more notable is the fact that the rate of progression appears to vary tremendously across subjects. V.A. was seen 3 years after initial symptoms appeared and within a year after that was too severely impaired to come to the hospital for testing and was fully unintelligible over the telephone. In contrast, E.G., over 15 years after initial symptoms, was still strong, performing volunteer work, and dropping by the author's office weekly to inquire after a potential cure for his problems. It is possible that the different rates of these two patients is related to their different symptom complexes and really represent two subgroups of the syndrome. There is some evidence from studies of Alzheimer's disease that individuals with extrapyramidal symptoms, in fact, form a subgroup that may differ in significant ways from those without motor impairment (Chui, Teng, Henderson, and May, 1985). Although only suggestive, in this series of three patients, the fastest rate of progression was associated with extrapyramidal symptoms, while the slowest rate was found in a man with fully intact motor functions. In sum, the rate of progression can be slow or fast, and associated symptoms such as parkinsonian features may, in the long run, be a predictor of progression rate or ultimate severity.

Previous reports of brain structure, function, and pathology have generally found (1) normal or mild left-sided atrophy on CT, (2) left-hemisphere slowing on electroencephalogram, (3) left-hemisphere focal temporal-parietal hypometabolism on PET, and (4) various degrees of plaques, neuronal depletion, atrophy, and spongiform degeneration of cortex on autopsy. We have presented CT and PET data from three additional cases, which essentially agree with past reports. Brain structure in
all three cases was similar: no evidence of defined structural damage, but some evidence of bilateral atrophy. This contrasts with previous case reports that identify predominately left-sided atrophy (or enlarged frontal horns, sylvian fissures, and so on) on CT (Gordon and Selnes, 1984; Mesulam, 1982; Morris et al., 1984). Brain function as measured by PET, demonstrated similarities and differences across cases. The common feature to all three cases was left temporal hypometabolism and essentially normal right-hemisphere function. Where each case differed was in the degree of hypometabolism in other (nontemporal) areas of the left hemisphere. The longest standing case with the slowest progression of symptoms (case 1) demonstrated the most circumscribed area of hypofunction, limited essentially to the left temporal lobe. The case with parkinsonian features (case 2) showed more widespread left-hemisphere hypofunction, including temporal, parietal, insular, thalamic, and caudate regions. It should be noted that these findings neither confirm nor rule out a diagnosis of Parkinson's disease. The PET pattern typically associated with Parkinson's disease is that of uniformly lower than normal measurements across all regions (e.g., Metter, Riege, Kameyama, Kuhl, and Phelps, 1984). The pattern observed in our patient shows slightly more focal findings than typical of Parkinson's disease but still we cannot rule out a diagnosis of Parkinson's disease on these findings alone. The final case, who demonstrated more global left-hemisphere symptoms, demonstrated depressed functions in all areas of the left hemisphere except the occipital lobe and the caudate.

Although, the neurological bases of these cases are still a mystery, the common finding of left temporal dysfunction in the absence of obvious structural damage is interesting in several respects. First, it confirms that observable structural brain damage is not prerequisite to persisting aphasic symptoms. Second, the common finding of metabolic disturbance suggests that brain dysfunction, without known structural damage, may manifest as persistent clinically significant aphasic symptoms. Third, it appears that brain dysfunction in the left temporal lobe affects behavior much like abnormalities of brain structure in the same regions. These findings support a neuropsychological model in which intact language function is correlated with not only a structurally intact perisylvian area, but also a functionally intact left temporoparietal area as well.

Finally, in describing these atypical cases of aphasia, it is important to remember that, at least with the cases presented here, each one is strikingly different from the other. These three cases, because of their distinct clinical pictures, may have different etiologies and different clinical courses. They do not constitute a coherent single syndrome. Patients diagnosed with "progressive aphasia" may well differ in the rate of symptom development and the extent to which deficits affect various
cognitive functions and motor speech production. These differences, in turn, will likely lead to different prognoses for maintaining speech and language functions. Realistic counseling and therapeutic efforts will be possible only after further detailed case histories of similar patients that will elucidate common and, we hope, predictable patterns in rate of progression and range of symptoms.

REFERENCES


**DISCUSSION**

**Q = question; A = answer; C = comments.**

**Q.** In patients who have slowly progressive neoplasms, there's some evidence to suggest (or at least theory) that maybe the right hemisphere starts functioning. Given the variability of the language samples here, given your 15-year-old case there, did you have any feeling for (we talk about hypometabolism on the left) hypermetabolism on the right; is such a thing measurable and do you have any feelings personally about that the scatter, like in that case one, might be due to the right hemisphere assuming some of those functions over a long term?

**A.** The right hemisphere in all these cases, and I apologise for not mentioning that earlier, is not significantly different than 22 normal controls. We could measure hypermetabolism, comparing it with normal controls, and these cases did not show that. Whether or not the right hemisphere is involved, I don't know. That one case, the first case, is interesting in that way because he seems to have focal language problems and a focal right-hemisphere problem in his face recognition deficit and he's also left-handed. So, I don't know. That's all I can say. The other two are right-handed.
Q. Just a terminological question. I had a conversation a couple of months ago with Marcel Mesalum about progressive aphasia, and I became fairly well convinced that it would be awfully nice to use that term to distinguish between those patients, who in fact develop dementias and those who in fact do not develop dementias. I think that’s the way in which a lot of individuals who write about this language disorder really tend to settle it. I just wonder how you feel about that, because obviously you’re on the other side of the argument, but I’m sort of interested in how you got there?

A. It’s very tricky, and one of the problems I see is in, obviously, defining dementia. We now have some criteria for Alzheimer’s disease, for probable Alzheimer’s disease before autopsy, which would include for some people deficits in three different cognitive domains. How do you define a cognitive domain? I don’t think any of these patients fit behavioral criteria for Alzheimer’s disease if we’re talking about Alzheimer’s.

C. Neither do half the patients in the literature who have progressive dementias fit Alzheimer’s disease. There are Pick’s disease patients in there; there are ALS patients in there, there are a whole bunch of other things, so I think it’s difficult to call all dementia Alzheimer’s disease.

A. Right. Joe Duffy last year made the point that I will make again, that if we look at aphasic patients, they also have nonlanguage symptoms. Are we going to call those dementias? Or are we going to call them aphasias? Just because they have some symptoms that are not strictly language doesn’t qualify them as a dementia. It’s terminological. I think clearly these cases can be more narrowly defined, with language being the predominant symptom throughout, and I think that’s the important point. I’d like to talk to Mesalum about these cases.

Q. I have a real fear that I’m being either picky, or naive and you can tell me which or both. But what does it mean to have done “OK” on the Raven’s or some of these other tests? Are you telling us that they got 100 percent correct?

A. They scored within either one or two standard deviations of age-matched controls. They were not out of the range of age-matched controls who were tested. Dr. Riege’s lab has tested thousands, or hundreds of control patients on all of these tests, and all of our patients, before he tells us whether they’re abnormal or low, are compared with his normal controls.

Q. So you’re making a judgment from that, that they have no non-language problems?
A. Well, that they perform the same as patients without known neurological deficit on that test.

Q. My question is a follow-up, but I think it's the other side of it. What do you consider aphasia? I don't have any problem with aphasics having nonverbal problems because they all do. I mean they always do if you look a little bit. But what do they have to be to be aphasic? I didn't see any of those guys who would meet my intuitive criteria for what aphasia is or must be. So I wonder if anybody ever attends to that. It's the issue that Jay brought up last night, and we always keep bringing up every year, every session: How do you define aphasia and what are your assumptions about its nature?

A. And we all have our own answers to that. Mine is that they do so much worse on language things than on other things. It's relative to their performance on other cognitive functions. I haven't been convinced that any other criteria are better. You know we can limit it to the neurology underlying it, we can say it has to be secondary to stroke or an infarct. And that would rule these fellows out. There are also similar issues in dementia. There are articles about "aphasia" in dementia. Well, is that aphasia? In those cases, I often come down and say "no." They have too many attentional problems, they have too many other things. We don't know whether the primary problem there is aphasia or not. It's not language.

Q. I have two questions, the first is kind of a follow-up and maybe a little less difficult to answer. If these patients have been sent to you and the referral said, "left hemisphere CVA with aphasia," "please evaluate," would you have been perplexed by their behavior or inconsistency with that clinical diagnosis?

A. Yes and no. Certainly in the first case, he was strange. He was not a typically aphasic CVA. In the last case, no, he sounded very much classically aphasic; anomic, paraphasias, that was all you could see going on. The middle case obviously had his dysarthria, so I would have been suspicious. So the answer is, I guess, yes, yes, no.

Q. The other question is, were any of these patients nonfluent or did they have an apraxia of speech? We've certainly been impressed by a substantial percentage of patients we've seen with slowly progressive speech and language difficulty as being in that nonfluent or apraxia of speech category. In fact, when we see that, it really makes us think something other than what the literature describes as someone with Alzheimer's disease.

A. No, these were more in keeping with the nonapraxic group.
C. Let me just make a comment on your question about presentation with stroke. The second patient presented was sent to me with a diagnosis of "unusual dysarthria." And the question was not whether he had a stroke, but what was the nature of his dysarthria. And what we found was that he had a severe hypokinetic dysarthria, he had a mild degree of rigidity, otherwise really didn't look parkinsonian at all. In addition, he had a severe anemia. And it was really the combination of severe dysarthria and anemia that became the issue. Over time the dysarthria remained the same, the anemia got progressively worse, he had increasing problems with language. This was a highly educated individual who used to drive 50 miles to see me, would come in with the Wall Street Journal and sit around waiting to see me reading the Wall Street Journal. After 2 years, he was no longer able to read a newspaper. After 3 years, he was no longer able, really, to come out and see me. No, he did not look at all like a stroke patient. Same with the first patient, he really looked, initially when we first saw him in '78, as though he might have had a stroke at that time, but he continued to progress and did not have the characteristic features because of the gradual progression of his disorder, which again was very much language, memory, and this issue of facial recognition. So I think the answer to your question is "no." The last case I only met one time. The opinion I had the one time I saw him was that this guy could have had a stroke, and he looked like an aphasic individual.

A. I think we all agree, that one out of three looked like a classic stroke aphasic patient.

Q. Do you think that for the benefit of future scholars it would be valuable to try to come up with an operational definition of "slowly progressive aphasia"? Would there be something to be gained for our scholarship by defining both "slowly" and "aphasia"? Perhaps, rather uniquely for this group?

A. Yes, I'll work on it.

Q. Would you like to show us the results of your early work right now? What is "slowly"? Is it possible that the variability in the patients in the literature reflects differences in the investigators rather than differences in the disorder of "slowly progressive aphasia"?

A. Well, there certainly are problems with definition. For instance, and I thank you all for not bringing this up, I only saw these patients one time. I saw them at 15 years, 5 years, and 3 years after their initial symptoms. I had medical records going back to the initial symptoms. Now that's a problem in the literature for defining "slowly." I was convinced because they had been seen by doctors that I knew and
trusted. These symptoms had been real, but they weren't given the Western Aphasia Battery every year. Obviously, that's the way to define "slowly" and "progressive" — how fast it goes, with testing every year at least. And that needs to be done. It's not done. There are very few serially studied cases like this. I think to define "slowly," I've given you my answer in that 3 years is slow because it doesn't happen overnight like a stroke, and 15 years is slower. We may have to have "not so slowly progressing aphasia," "medium slowly progressing aphasia," and "very slowly progressing aphasia." We need more data.