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PRIMARY PROGRESSIVE APHASIA

Analisys of 16 cases

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ABSTRACT - Primary progressive aphasia (PPA) is an intriguing syndrome, showing some peculiar aspects that differentiate it from classical aphasic pictures caused by focal cerebral lesions or dementia. The slow and progressive deterioration of language occurring in these cases provides an interesting model to better understand the mechanisms involved in the linguistic process. We describe clinical and neuroimaging aspects found in 16 cases of PPA. Our patients underwent language and neuropsychological evaluation, magnetic resonance imaging (MRI) and single photon emission computerized tomography (SPECT). We observed a clear distinction in oral expression patterns; patients were classified as fluent and nonfluent. Anomia was the earliest and most evident symptom in both groups. Neuroimaging pointed to SPECT as a valuable instrument in guiding the differential diagnosis, as well as in making useful clinical and anatomical correlations. This report and a comparison to literature are an attempt to contribute to a better understanding of PPA.

KEY WORDS: primary progressive aphasia, focal cortical degeneration, cerebral perfusion, neuroimaging.

Afasia progressiva primária: análise de 16 casos

RESUMO - A afasia progressiva primária (APP) é uma síndrome que tem despertado grande interesse devido a aspectos particulares que a diferenciam das afasias clássicas (secundárias a lesões cerebrais focais) e dos quadros demenciais. A deterioração lenta e progressiva da linguagem presente nesses casos fornece um interessante modelo de observação dos mecanismos subjacentes ao processamento linguístico. Descrevemos as características clínicas e de neuroimagem de 16 casos de APP. Os pacientes foram submetidos a exame de linguagem, neuropsicológico, ressonância magnética (RM) e tomografia computadorizada por emissão de fóton único (SPECT). Clinicamente pudemos observar uma nítida distinção nos padrões de produção oral, sendo os pacientes agrupados em fluentes e não-fluentes. Anomia foi o sintoma mais precoce e evidente nos dois subgrupos. Os achados de neuroimagem permitem destacar a sensibilidade do SPECT como instrumento diagnóstico. O registro e a comparação destes casos aos da literatura são uma tentativa de contribuir para a compreensão da APP.

PALAVRAS-CHAVE: afasia progressiva primária, degeneração focal cortical, perfusão cerebral, neuroimagem.

Progressive language impairment in patients with relative preservation of other cognitive functions is called primary progressive aphasia (PPA); it is a clinical syndrome with several aspects still open to question, for example language profile characterization and clinical and neuroimaging diagnostic criteria.

The first description of isolated progressive loss of language was reported by Pick, in 1892[1], describing a patient with severe language disturbance associated with atrophy in the left temporo-polar region and posterior two thirds of the frontal lobe. Later, the same author described other patients with temporal[2], parietal and frontal lobe atrophy[3]. The term "Pick's disease" was later used for any similar progressive atrophic diseases, especially those with predominant behavioral disturbances. Other authors have also described predominant language alterations, under the name "aphasic dementia" or "pure verbal deafness evolving to sensorial aphasia"[4-6]. Perhaps due to greater frequency, Alzheimer's dis-

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ease was liberally diagnosed to many clinical conditions, including those that could be considered PPA.

In 1982, Mesulam[7] described six patients with isolated and long lasting language deterioration, naming these clinical pictures as slowly progressive aphasia without dementia, later called PPA. Some of these patients, in spite of serious limitations to oral and written communication, were able to maintain autonomy in daily life activities. More than a hundred similar cases have been reported in literature[8]. In Brazil, Oliveira et al.[9] were the first to report a case of PPA.

To date, some 33 cases of PPA have undergone pathologic examination, showing predominantly (in approximately 60% of cases) signs of non-specific focal degeneration with neuronal loss, gliosis and spongiform alterations in superficial cortical layers[10-12]. Alterations compatible with Pick's disease were seen in about 20% of the patients[13-15], whereas the remaining 20% had Alzheimer's disease[16]. There is a report of Creutzfeldt-Jakob disease manifesting itself as PPA in its fluent form[17]. It is nowadays accepted that PPA constitutes a syndrome including different etiologies and whose diagnosis is clinical and based on the presence of progressive language deficit, which during the first two years is either the only affected cognitive function or is the most important function involved. Although usually isolated, PPA may coexist with disorders such as acalculia, ideomotor or constructional apraxia, indicative of left hemisphere damage[18,8]. These clinical manifestations emerge in the absence of morphologic alterations (excluding atrophy) both in computerized tomography (CT) and magnetic resonance imaging (MRI). Atrophy usually appears in left frontal, temporal or perisylvian cortices[19].

Clinical presentations similar to PPA can occasionally be found such as in pure progressive verbal deafness, described in a patient with left superior temporal atrophy[20] and pure progressive aphemia[21].

The purpose of this paper is to report clinical, linguistic and neuroimaging characteristics found in 16 PPA cases diagnosed and accompanied by the Behavioral and Cognitive Neurology Unit of the Neurological Division, Hospital das Clínicas of the University of São Paulo School of Medicine.

METHOD

Sixteen patients were studied, whose demographic data are presented in Table 1. Language evaluation was performed using Montreal-Toulouse (BETA version)[22] and Boston Diagnostic Aphasia Examination (BDAE)[23] protocols, with patients classified as fluent and nonfluent. Seven patients were evaluated longitudinally. The remaining cognitive functions were evaluated using the Mini-Mental State Examination (MMSE)[24] and complementary neuropsychological tests. Cranial MRI was performed on all patients. Ten patients were also submitted to single photon emission computerized tomography (SPECT).

RESULTS

Our series comprised nine females and seven males, with ages varying between 39 and 83 years (average 62.8 years) and an educational level between two and 20 years (average 10.7 years). Six patients spoke other languages besides Portuguese (see Table 1). Neuropsychological evaluation results are shown in Table 2. Performance in language tests, repeated after a one to two year interval in seven cases, is presented in Table 3. Neuroimaging exam results are described in Table 4.

Figure 1 shows a comparison in language performances between fluent and nonfluent groups. Figures 2 and 3 show the speech characteristics profile scales for each group and its evolution over time. These profiles are useful in identifying similarities and differences between fluent form and Broca's aphasia (Fig 2) or between nonfluent form and Wernicke's aphasia (Fig 3). Figures 4 and 5 illustrate the neuroimaging (SPECT and MRI) findings in a fluent and a nonfluent patient, respectively. These figures include speech samples from the same patients.

Differential diagnosis and evolution of cases

The clinical course, although restricted in some cases, can cast further light on the differential diagnosis between correlate syndromes such as semantic dementia, as observed in case 14.

In this case, the family's report on the progression of linguistic changes suggests steady reduction, and their first description approached transcortical motor aphasia. Oral comprehension began worsening three years after the disease had manifested, where aspects most preserved were word repetition and reading. The patient's evolution showed marked comprehension difficulties, which differentiates it from a typical anterior cerebral lesion profile. In this case, one can speculate on the presence of semantic dementia (given that the family's description of language reduction was somewhat vague). This hypothesis does not persist given the verification of a residual comprehension capacity, aptitude for isolated words in naming tests and also evidenced by the ability to treat information semantically when visual stimuli were supplied, such as in reading tests. Besides, there were no difficulties in manipulating objects.

Table 1. Demographic data and presenting symptoms.

Patient	Age	schooling (years)	ΔT 1st eval (months)	Language	presenting problem
1	82	9	18	Portuguese	naming
2	52	15	60	Portuguese	naming
3	63	5	24	Portuguese	naming
4	45	11	60	Portuguese	"asking strange questions and forgetting the answers"
5	77	15	18	Czech Portuguese	recent memory word finding
6	59	15	24	Spanish Portuguese	word finding
7	72	9	18	Portuguese	expression and word finding
8	72	5	24	Portuguese	word finding
9	70	16	30	Italian Portuguese	naming: proper names
10	60	20	12	Portuguese Japanese	word finding
11	67	11	48	Portuguese	expression memory loss depression
12	60	11	24	Portuguese	"forgetfulness" word finding
13	39	11	72	Norwegian Portuguese	writing
14	60	2	48	Portuguese Spanish	expression in Spanish (mother tongue) and slowness in Portuguese
15	68	4	24	Portuguese	oral production oral and speech apraxia
16	60	12	24	Portuguese English	"stuttering" expression difficulties

ΔT 1st eval : time from onset of symptoms to first evaluation

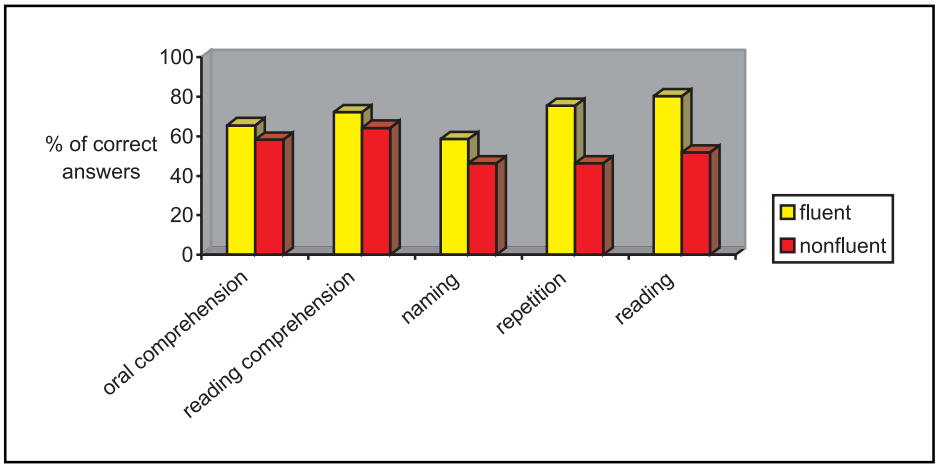


Fig 1. Average performance on language tests.

Table 2. Neuropsychological evaluation and deficit evolution.

Patient	MMSE / NP alterations (first evaluation)	deficit evolution
1	NT / mild memory impairment	oral comprehension and reading after one year
2	22 / verbal and non-verbal memory	oral comprehension after one year memory, apathy, irritability, obsessive behavior after five years FTD after eight years
3	9/ digit span	anomia
4	9/ memory, digit span and calculation	pragmatic communication disturbance
5	20 / normal	oral comprehension depression
6	26 / verbal memory	anomia
7	22 / NT	memory transient behavioral disturbances (nocturnal fears, "strangeness of environment") after three years
8	25/ NT	recent memory
9	23 / anterograde episodic memory and visuospatial abilities	naming in general
10	22 / initiation, perseveration, verbal and visual memory and conceptualization	reading and calculation impaired lexical access, phrase reformulation
11	12 / Mattis[34]: 87/144 (attention, memory, constructional praxis and executive functions)	symptoms worsening
12	25/ Mattis: 116/144 (executive functions and verbal episodic memory)	agraphia slowness in talking
13	24 / constructional praxis, acalculia and non-verbal memory	agraphia after four years expression and recent memory after five years
14	NT / normal	oral production in both languages
15	29 / normal	dementia after five years
16	20/ Mattis: 97/144 (attention, constructional praxis and executive functions)	expression difficulties worsening

NP: neuropsychological evaluation; NT: not tested; FTD: frontotemporal dementia.

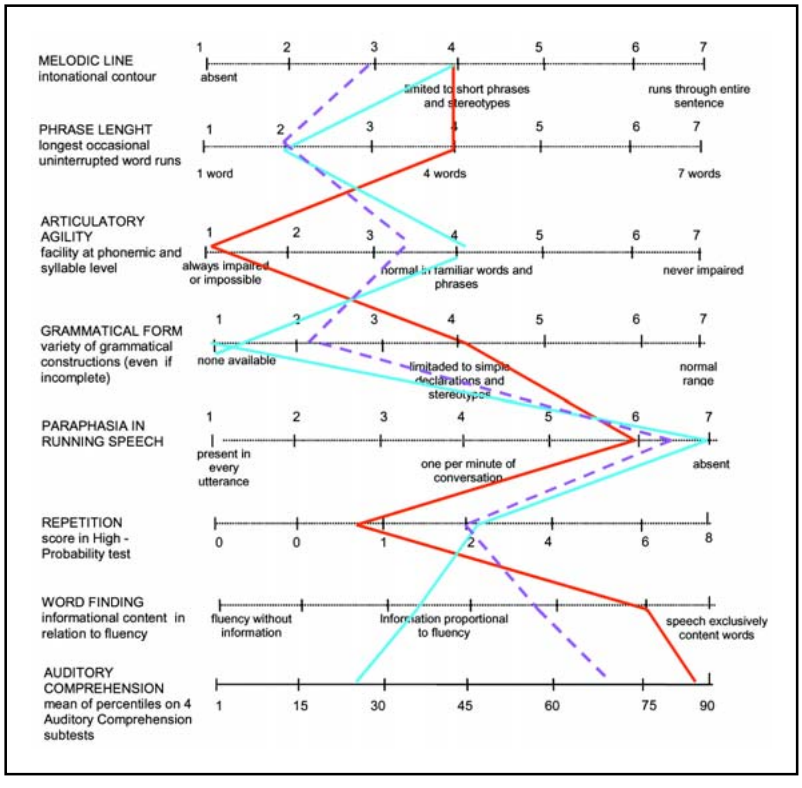


Fig 2. Speech characteristics profile scale (Goodglass and Kaplan, 1985). PPA patients, nonfluent form. Red line: patient with less than 36 months of disease; blue line: average for patients with more than 36 months of disease; dotted line: Broca's aphasia profile.

Table 3. Language examination. Performance in tests is expressed in terms of percentage of correct answers.

Patient	fluency	Δt (yrs)	oral compr	reading compr	naming	repetition	reading	writing (dictate)	protocol
1	F	1	73.3	46.7	70.9	78.7	100	53.8	Beta
			62.5	69.2	66.6	86.6	86.6	ND	Beta
2	F	2	86	75	24	90	70	85	Beta
			49.1	55	8.3	93.3	53.3	ND	Beta
3	F	1	21.4	40	43	62.5	60	42.7	BDAE
			36.2	61.5	35.5	90.9	81.8	ND	Beta
4	F	NA	26.1	30	45.8	54.3	40	0	BDAE
5	F	NA	52.5	59.5	11.7	45.8	100	55,7	Beta / BN
6	F	NA	97.2	100	94.5	91.6	100	96.6	BDAE
7	F	1	86.3	85	92	82.5	100	84.7	Beta
			75.3	68.3	56.6	62.5	82.5	64.5	BDAE
8	F	NA	100	100	84	100	100	ND	Beta
9	F	NA	96.3	68.3	64	100	96.7	ND	Beta
10	F	NA	97.2	90	86.7	42.5	66.7	42.3	BDAE
11	F	NA	87.7	73	13.8	66.6	55.5	ND	Beta / BN
12	F	1	76.6	89.5	66.7	97.8	100	92.7	Beta
			84.8	91.66	75	70.8	100	88.2	Beta
13	NF	1	60.9	75	49.3	57.8	74.5	0	Beta
			59.6	58.9	76	62.3	55	0	Beta
14	NF	NA	28.3	36.6	2.75	43.3	13.3	0	BDAE
15	NF	2	100	100	100	100	100	ND	Beta
			87	87	78	48	45	ND	Beta
16	NF	NA	68.3	47	28.3	31.1	93.7	ND	Beta / BN

Δt: interval between first and second evaluation ; compr: comprehension; NA: not applicable; ND: not done; BN: Boston naming test.

Neuroimaging

Considering the MRI findings, we noted that 15 patients in our series presented predominant left hemisphere atrophy. In three cases (2, 4 and 16), the atrophy was bilateral, although predominant in the left side. The temporal region was the most affected, with atrophy present in 11 cases; one with temporo-parietal atrophy (Case 6), two with fronto-temporal atrophy (Cases 15 and 16) and one with volumetric reduction of left hippocampus (Case 5). Perisylvian atrophy was reported in three cases (1, 7 e 8), thus implying frontal and/or temporal degeneration (these cases are considered separately because we can not describe the site of anomaly accurately). One case (13) presented diffuse cortical and subcortical atrophy.

Regarding perfusion studied with SPECT, of the 13 patients that underwent the exam, ten presented CBF abnormalities in the left hemisphere only. Bilateral CBF abnormalities existed in Cases 4, 13 and 16, being focal in two cases (4 and 16) and generalized in one (13). In eight cases, the temporal region was the most affected, being isolated in one case (2), or associated with frontal (Cases 3 and 14), parietal (Cases 7, 10 and 16) or fronto-parietal (cases 5 and 12). Three patients had homogeneous left fronto-temporo-parietal CBF abnormalities (Cases 6, 11 and 15). The perfusion abnormalities were more pronounced than those found in MRI, both in extension and intensity.

Table 4. Neuroimaging results.

Patient	MRI	SPECT
1	mild asymmetry of sylvian fissures (L > R)	not performed
2	diffuse atrophy, mainly in left temporal region	left temporal hypo perfusion
3	sectorial enlargement of left insular cistern and enlargement of cortical sulci in left temporal region	left temporal hypo perfusion with mild left frontal extension
4	mild cortico-subcortical atrophy slightly larger on left side	left parietal and occipital hypo perfusion plus right parietal
5	left cortical atrophy / left hippocampal volumetric reduction	severe left temporal hypo perfusion with left frontal and parietal extension
6	left inferior parietal and temporal atrophy	left fronto-temporo-parietal hypo perfusion
7	ventricular asymmetry (L > R)	left temporo-parietal hypo perfusion
8	ventricular asymmetry (L > R)	not performed
9	left temporal atrophy	not performed
10	left temporo-parietal atrophy	left temporo-parietal hypo perfusion
11	left temporal atrophy	moderate left fronto-temporo-parietal
12	left temporal atrophy	left fronto-parietal, anterior temporal and basal ganglia hypo perfusion
13	cortico-subcortical atrophy	bi-hemispheric hypo perfusion, mainly on left side
14	severe hemispheric asymmetry with left temporal atrophy	left temporal hypo perfusion with mild left frontal extension
15	left fronto-temporal atrophy	left fronto-temporo-parietal hypo perfusion
16	bilateral cortical atrophy, predominating in left fronto-temporal region	left mesial temporal and bilateral parietal hypo perfusion

L: left; R: right

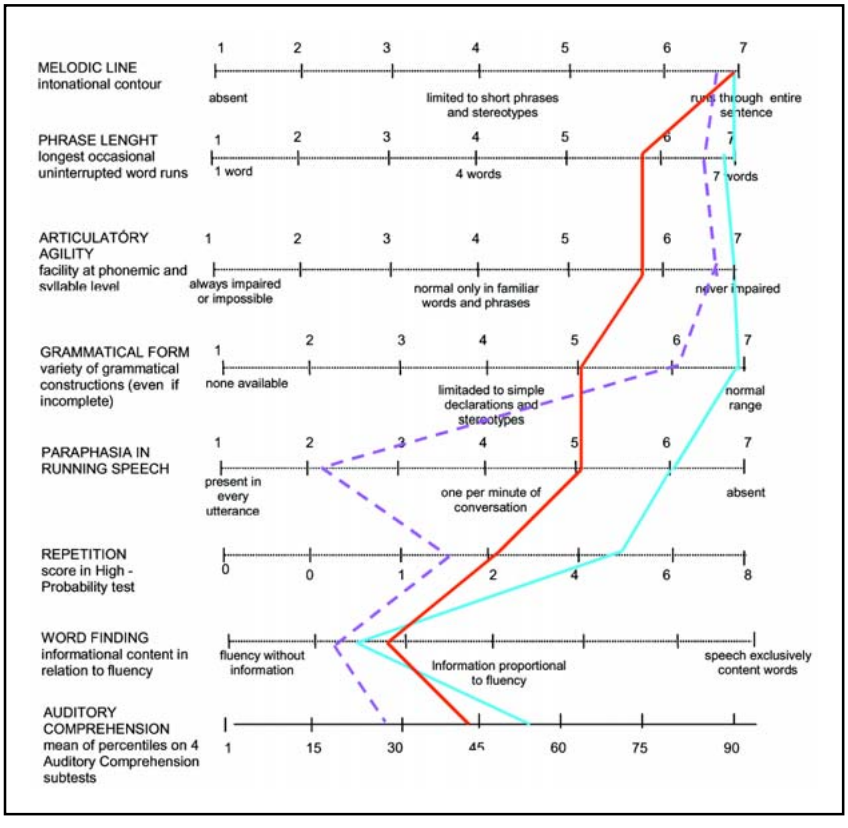
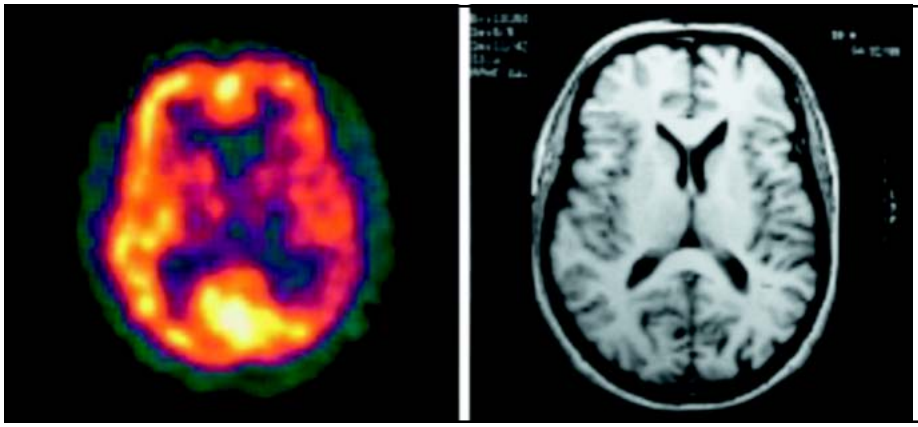


Fig 3. Speech characteristics profile scale (Goodglass and Kaplan, 1985). PPA patients, fluent form. Red line: average for two patients with less than 36 months of disease; blue line: average for patients with more than 36 months of disease; dotted line: Wernicke's aphasia profile.

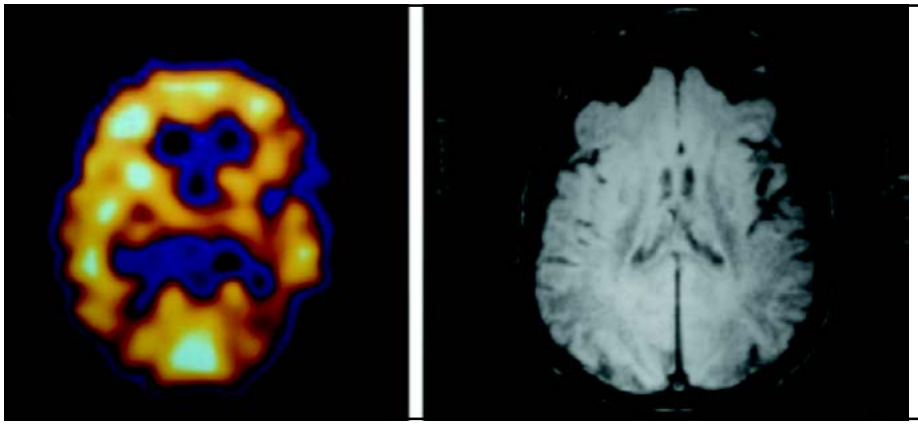


Impairment of lexical access in a fluent patient (case 6)

P – My apartment has 3 rooms has a... has a big living room, has a big *sacada* with a...*churrasqueira* that is to keep Argentine habits. It has a kitchen, it has a small room for breakfeast and also when we are alone we use it as...as...to have lunch and dinner...

The words in italic refer to names that the patient couldn't access in his mother tongue (Spanish) and were spoken in Portuguese.

Fig 4. Case 6 - SPECT and MRI showing mild hypoperfusion and atrophy in left parieto-temporal region.



Agrammatism found in a nonfluent patient (case 15)

Illustrations sequence: in this story, a woman leaves her car with two children inside. The children start driving and the car crashes in a lamppost.

Patient's description:
car guide *womun* (woman)
car exits *womun*
car break fall
car fall break
the boy guide *aumobile* (automobile)
womun.. (unintelligible).. *count* (crash) *pasts* (posts)
womun beak (break)

Fig 5. Case 15 - SPECT and MRI showing mild hypoperfusion and atrophy in left fronto-temporal region

DISCUSSION

Our results disclosed different and peculiar patterns of language impairment among the patients, to be expected, especially considering the differing progressions of the disease over time. The anatomical distribution of abnormalities in neuroimaging is similar to that described in literature .

The first possible consideration, analyzing language data, is including these cases in the classical aphasic syndromes. Using generic taxonomy, we chose to divide the cases into fluent and nonfluent and to identify the isolated aphasic symptoms, given that one of the difficulties in regard to classification, stems from the fact that the patients were diagnosed when the intensity, combination and sum of alterations surpassed the classical aphasic syndrome definitions. The attempt to recoup evolution from clinical history provided by family proved unsuccessful, given the overlapping interpretations of memory and language alterations, exemplified by frequent indications of "word forgetting" for anomia, or the generic descriptions of "pronunciation alterations".

As new cases of PPA were being described, it became evident that the clinical features are complex and heterogeneous. This has led several authors to attempt a classification of the patients into subgroups with similar clinical characteristics. One of the first attempts was to categorize into nonfluent (where expression alterations such as agrammatism, emission reduction and phonologic alterations predominate) and fluent, where the semantic impairment is more evident. One of the most intriguing discussions arises from similarities and differences that may exist between fluent PPA and "semantic dementia"[25,26]. In the latter condition, however, the impairment of cognition seems to be more prevalent, affecting the recognition of words and objects, traits usually associated with bilateral temporal lobe dysfunction.

The subdivision into nonfluent and fluent groups proved insufficient to include all new data observed by researchers. Principally due to the overlapping of symptoms between patients in both groups, as well as features shared by PPA and other degenerative diseases with lobar atrophy, such as frontotemporal dementia (FTD) [27,25]. The existence of pathologic alterations that are present both in FTD and PPA reinforces the hypothesis of both manifestations representing a non-Alzheimer degenerative process, with the occurrence of a different distribution of the pa-

thological process, either predominantly in the frontal or temporal lobes. Due to this overlapping of clinical and pathological characteristics, Kertesz et al. [28,29] proposed the term "Pick complex" to include the clinical conditions currently described as FTD, PPA, Pick's disease and corticobasal degeneration.

Weintraub and Mesulam[30] proposed a classification of degenerative dementia based on four clinical profiles, each in turn having more probability of association with a specific cerebral disease. This classification takes into account the neuropsychological profile exhibited by the patient during the first two years of disease. PPA is one of these profiles (Progressive Language Network Syndrome).

In our series, it was not possible to classify the patients into classical aphasic syndromes, although a resemblance to predominantly frontal dysfunction (agrammatism), or temporal (marked comprehension disturbances) is admissible. That said, symptoms also described in dementia occurred alongside the language primary deficit.

Regarding fluency, which is a referential for subgroup identification, we did not notice any remarkably positive characteristics, such as hyper fluency. Reduction in fluency and quantitative emission predominated, and were shared by the patients with clinical symptoms compatible with both frontal and temporal dysfunction. Absence of language production occurred when extra-language cognitive symptoms intensified. Anomia was the earliest and most notable symptom, being present in all patients. Disturbances of repetition were also frequent and could be found in the fluent and nonfluent groups.

We can notice in Figures 2 and 3 that the nonfluent group presents greater similarities to Broca's aphasia profile as the disease evolves, except for comprehension, which is more impaired in our data. In the fluent group, independent of evolution time, the profile is more akin to that found in Wernicke's aphasia, except for the occurrence of fewer semantic paraphasias in language production.

One of the main goals in the research field of degenerative cerebral diseases is to find a method with enough specificity to allow the elaboration of a prognosis, bearing in mind the great number of years necessary to reach a clinical diagnosis with reasonable acuity. Toward this goal, several groups have striven to establish relations between perfusion and neuroimaging, and the probable clinical evolution for each profile. Talbot et al.[31] described the correlation between standard perfusion with SPECT in 363 patients studied prospectively for 3 years. They found positive correlation between the presence of posterior bilateral alterations and Alzheimer's disease, and between anterior bilateral alterations and FTD. Other perfusion patterns, such as patchy distribution and generalized or unilateral (anterior or posterior) alterations, showed less correlation and therefore were less useful for the characterization of a diagnosis.

Neuroimaging findings in PPA keep certain correlation with the clinical variant. In nonfluent cases, there is left frontal and perisylvian atrophy in cranial CT and MRI, with CBF abnormalities in the same areas in SPECT. In fluent cases, the cortical atrophy and CBF abnormalities are located predominantly in the left temporal lobe, hippocampus and parahippocampal gyrus[32]. In a review article of 112 cases, Westbury and Bub[33] found the following distribution: of 59 cases that performed PET or SPECT, 39 (66.1%) had CBF abnormalities exclusively in the left hemisphere and 18 (30.5%) had bilateral CBF abnormalities; perfusion was normal only in two cases (3.4%). In the left hemisphere, for 27.3% of cases the CBF abnormalities were located in the fronto-temporal region, 21.2% in the temporal region, 12.1% in the frontal region, and the remaining 39.4% were distributed between frontal, temporal and parietal lesions combined. In those cases for which MRI was performed (105), 49 (46.7%) had atrophy in the left side only, 38 (36.2%) had bilateral atrophy and in 17 (16.2%) the exams were normal.

The anatomical distribution found in our cases was similar to that documented in literature, namely: predominance in the left hemisphere and, within this, in the temporal and frontal regions or combination of the two. We observed that the abnormalities were more apparent in SPECT than in MRI findings, generally showing areas of CBF abnormalities that were larger and more evident than those seen in MRI. We think this feature of SPECT might be helpful, especially in the earlier stages of the disease when MRI shows only mild diffuse atrophy or asymmetry of Sylvian fissures, in providing a useful clue for correct diagnosis.

CONCLUSION

We found elements in our series that suggest the need to seek an analysis model for the clinical picture of PPA. We think that the description of symptomatology from a longitudinal and cross-sectional point of view is very important to improve our ability to diagnose PPA in its initial phase. Moreover, it will allow refinement of the tools used to identify

the symptoms that are typical of this phase. Furthermore, this description can aid to identification of those symptoms that overlap in language disorders and other cognitive losses. Regarding the neuroimaging exams, we believe that SPECT is a valuable instrument in guiding the differential diagnosis, as well as in making useful clinical and anatomical correlations.

REFERENCES

1. Pick A. Über die Beziehungen der senilen Hirnatrophie zur Aphasie. Prager Med Wochenschr 1892;17:165-167 apud Poeck K, Luzzatti C, 1988:160.
2. Pick A. Zur Symptomatologie der linksseitigen Schläfenlappenatrophie. Monatsschr Psychiatr Neurol 1904;16:378-388 apud Poeck K, Luzzatti C, 1988:160.
3. Pick A. Über einen weiteren Symptomenkomplex im Rahmen der Dementia senilis, bedingt durch umschriebene stärkere Hirnatrophie (gemischte Apraxie). Monatsschr Psychiatr Neurol 1906;19:97-108 apud Poeck K, Luzzatti C, 1988:160.
4. Sérieux P. Sur un cas de surdité verbale pure. Rev Med 1893;13:733-750.
5. Franceschi F. Gliosi perivascolare in un caso di demenza afasica. Annali di Nevrologia 1908; 26:281-290 apud Poeck K, Luzzatti C, 1988:160.
6. Mingazzini G. On aphasia due to atrophy of the cerebral convolutions. Brain 1914; 36:493-524 apud Poeck K, Luzzatti C, 1988:160.
7. Mesulam MM. Slowly progressive aphasia without generalized dementia. Ann Neurol 1982;11:592-598.
8. Mesulam MM. Aging, Alzheimer's disease, and dementia. In Mesulam MM (ed) Principles of behavioral and cognitive neurology. 2.Ed. New York: Oxford University Press, 2000: 455-458.
9. Oliveira SAV, Castro MJO, Bittencourt PRM. Slowly progressive aphasia followed by Alzheimer's dementia. Arq Neuropsiquiatr 1989;47:72-75.
10. Kirshner HS, Tanridag A, Thurman L, Whetsell WO Jr. Progressive aphasia without dementia: two cases with focal spongiform degeneration. Ann Neurol 1987;22:527-532.
11. Lippa CF, Cohen R, Smith TW, Drachman D. Primary progressive aphasia with focal neuronal achromasia. Neurology 1991;41:882-886.
12. Deruaz JP, Assal G, Peter-Favre C. Un cas clinico-pathologique d'aphasie progressive. Rev Neurol (Paris) 1993;149:186-191.
13. Holland Al, McBurney DH, Moosey J, Reinmuth OM. The dissolution of language in Pick's disease with neurofibrillary tangles: marries her study. Brain Lang 1985;24:36-58.
14. Graff-Radford NR, Damasio AR, Hyman BT, Hart MN, Tranel D, Damasio H et al. Progressive aphasia in patient with Pick's disease: neuropsychological, radiologic, and anatomic study. Neurology 1990;40:620-626.
15. Kertesz A, Munoz D. Clinical and pathological characteristics of primary progressive aphasia and frontal dementia. J Neurol Transm Suppl 1996;47:133-141.
16. Kempler D, Metter EJ, Riege WH, Jackson CA, Benson DF, Hanson WR. Slowly progressive aphasia: three cases with language, memory, CT and PET data. J Neurol Neurosurg Psychiatry 1990;53:987-993.
17. Mandell AM, Alexander MP, Carpenter S. Creutzfeldt-Jakob disease presenting isolated aphasia. Neurology 1989;39:55-58.
18. Poeck K, Luzzatti C. Slowly progressive aphasia in three patients – the problem of accompanying neuropsychological deficit. Brain 1988;111: 151-168.
19. Turner RS, Kenyon LC, Trojanowsky JQ, Gonatas, N, Grossman, M. Clinical, neuroimaging, and pathologic features of progressive nonfluent aphasia. Ann Neurol 1996;39:166-173.
20. Otsuki M, Sum Y, Sato M, Homma A, Tsuji S. Slowly progressive pure word deafness. Eur Neurol 1998;39:135-140.
21. Cohen L, Benoit N, Van Eeckhout P, Ducarne B, Brunet P. Pure progressive aphemia. J Neurol Neurosurg Psychiatry 1993;56:923-924.
22. Nespoulous JL, Lecours AR, Lafond D, Reads May A, Puel M, Joanette Y et al. Protocole Montreal-Toulouse d'examen linguistique of l'Aphasie: module standard initial (version Beta). Montréal: Laboratoire Théophile-Alajouanine, 1986.
23. Goodglass H, Kaplan E. The assessment of aphasia and related disorders. 2.Ed. Malvern: Lea & Fabiger; 1983.
24. Folstein MF, Folstein IF, McHugh PR. Mini-mental state. J Psychiatr Res 1975;12:189-198.
25. Snowden JS, Griffiths HL, Neary D. Progressive language disorder associated with frontal lobe degeneration. Neurocase 1996;2:429-440.
26. Hodges JR, Garrard P, Patterson K. Semantic dementia. In Kertesz A, Munoz DG. (eds). Pick'd disease and Pick complex. Wiley-Liss, 1998:83-103.
27. Snowden JS, Neary D. Progressive language dysfunction and lobar atrophy. Dementia 1993;4:226-231.
28. Kertesz A, Hudson L, Mackenzie IRA, Munor DG. The pathology and nosology of primary progressive aphasia. Neurology 1994;44:2065-2072.
29. Kertesz A, Davidson W, Munoz DG. Clinical and pathological overlap between frontotemporal dementia, primary progressive aphasia and corticobasal degeneration: Pick complex. Dement Geriatr Cogn Disord 1999;10:45-49.
30. Weintraub S, Mesulam MM. Four neuropsychological profiles in dementia. In Boller F, Grafman J (eds.). Handbook of Neuropsychology. Amsterdam: Elsevier, 1993;8:253-282.
31. Talbot PR, Lloyd JJ, Snowden JS, Neary D, Testa HJ. A clinical role for ^{99}Tc-HMPAO SPECT in investigation of dementia? J Neurol Neurosurg Psychiatry 1998;64:306-313.
32. Abe K, Ukita H, Yamagihara T. Imaging in primary progressive aphasia. Neuroradiology 1997;39:556-559.
33. Westbury C, Bub D. Primary progressive aphasia: review of 112 cases. Brain Lang 1997;60:381-406.
34. Mattis S. Dementia rating scale: professional manual. Odessa: Psychological Assessment Resources, 1988.