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ORIGINAL PAPER

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Frontal lobe degeneration of non-Alzheimer type and Pick's atrophy: lumping or splitting?

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Abstract We report six cases of presenile (five) and senile (one) progressive dementia with a mild-to-marked frontal or frontotemporal atrophy and ventricular dilation (Frontal Lobe Degeneration [FLD]). The most prominent microscopic features were layer-dependet neuronal depletion of the cortex. spongiosis, and cortical and subcortical gliosis. Five cases showed additional degeneration of the S. nigra, and two also had motor neuron disease. Despite the absence of Pick cells and bodies, such cases have many features in common with Pick atrophy. Because Pick cells and bodies are inconstantly occurring features in otherwise typical cases of Pick atrophy, they cannot be regarded as inevitable markers of the latter. In our opinion, cases with mild frontal or frontotemporal atrophy as described herein and by others match the grades 1 and 2 in terms of Schneider's classification of Pick atrophy [37]. As long as the etiology of both Pick atrophy and the so-called FLD is unknown, and we finally have to follow morphological criteria for classification, there is apparently no convincing reason to introduce a separate category, such as FLD or FTA, for the cases with moderate or mild frontal atrophy and dementia of frontal lobe type, which can be sufficiently classified with the Pick spectrum of lobar atrophy.

Key words Frontal lobe degeneration · Dementia · Non-Alzheimer type

Introduction

Since Arnold Pick's first descriptions of the lobar atrophies with progressive dementia [32–35], these forms of late-life dementia became well characterized clinically and morphologically by reports in the literature of more than 300 cases [1, 2, 5, 8, 18, 21, 24, 40]. They entered the textbooks under the terms Pick atrohpy of Pick disease [12]. Several years ago Brun [6] and Gustafson [13] drew attention to a group of cases of progressive dementia occurring with frontally pronounced focal brain atrophy, which histologically were neither characterized by Alzheimer-type pathology (plaques, tangles, vascular amyloid) nor by cortical Lewy bodies or by Pick cells and Pick bodies. The latter are frequently considered to be markers of the fronto- and temporolobar atrophy first described by Pick ("typical Pick disease" [8]) [34, 35].

Morphologically, the brains in Brun's [6] and Gustafson's [13] cases were characterized by a mild-to-moderate frontal or fronto-temporo-polar atrophy instead of the severe "knife-blade atrophy" of typical Pick atrophy. Microscopically, they showed neuronal loss and spongiosis most pronounced in the upper cortical layers, and fibrillary gliosis, but no Pick cells and Pick bodies [6, 7].

In a series of 158 consecutive cases from a clinico-morphological long-term study with an 80% autopsy rate 16 (10%) such cases were found. Only 4 (2.5%) showed the typical gross and microscopic features of Pick atrophy [6, 13]. Jellinger and Bancher [19] found 4 cases with moderate frontal lobe degeneration and 10 with typical Pick disease in a consecutive autopsy series of 1200 demented patients.

Further observations of mild frontotemporal atrophy with dementia were thenceforth described [9, 17, 20, 26–29]. In some of them frontal lobe atrophy was combined with clinical and morphological sings of motor neuron disease and Parkinsonism with degeneration of the S. nigra. Similar combinations had already previously been reported in cases with typical Pick atrophy [21, 25, 31].

Brun [6] and Gustafson [13] as with the Manchester group [26–29], conceived that they were dealing with a subgroup of focal brain atrophy of frontal or frontotemporal distribution, which could be separated from the spectrum of Pick atrophy. Terms such as FLD of non-Alzheimer type [6, 7, 13,], dementia of frontal lobe type

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(DFT) [28, 29], frontotemporal dementia (FTD) [39], non-transmissible spongiform encephalopathy [26], or progressive lobar atrophy [26] were coined.

Apart from the lobar atrophy, all such cases have in common that the progressive dementia is microscopically not classifiable due to the absence in routine stainings of any typical microscopic markers in the cortex.

In the present paper six cases of presenile ($n = 5$) or senile ($n = 1$) dementia observed at the Institute of Neuropathology of the University of Heidelberg in the years 1976–1992 provide a basis for discussion of the problem of whether such cases can really be considered to represent a subgroup among the dementias with lobar atrophy, or whether they should be included in the spectrum of Pick atrophy.

Case reports

Case 1

A 33-year-old professional car driver was involved in a traffic accident where he sustained a scalp wound and thoracic and shoulder contusion. He did not become unconscious. Upon admission to the hospital he was fully oriented. There was no amnesia. Soon after, his wife realized that he became increasingly disinterested, apathetic, and withdrawn from his family. He often did meaningless repetitive things and tended to perseverate and to recite childish phrases. He often behaved impudently and echoed what other people said (echolalia). His capacity to manage work decreased significantly. He sustained further accidents with injuries of the arms and legs, about which he was unconcerned. A year and a half after the onset of psychiatric symptoms he lost his job; however, he did not take this seriously and made no efforts to find other employment.

About 2 years after the onset he had to be admitted to a psychiatric hospital. Upon admission he was fully oriented to time, person, and location. Upon medical examination he appeared agitated, restless, irritable, suspicious, and unconcentrated. He suddenly began to recite a poem or count things in his environment. He completely lacked insight into his disorder and showed no emotional reactions. His memory was undisturbed. There were no delusions or hallucinations.

Psychometeric testing revealed an IQ of 88 (percent rank 10–25), with a better verbal but decreased performance score in the Hamburg-Wechsler test. With the "Aufmerksamkeits-Belastungstest" (letter canceling test; d2) the percent rank was below 10. Rosenzweig's Picture Frustration test could not be performed because the patient was too unconcentrated and uncooperative, and he ran away shortly after the beginning of the test.

Later, he became increasingly lethargic, most of the time lying apathetically on his bed. Occasionally, he developed sudden episodes of aggression and tended to beat his wife or sleeping patients. He did not show any emotion and no regret. He sometimes displayed catatonic spells, remaining in a rigid posture for several minutes. Eventually, he became completely mute. Computer tomography scans of his head displayed marked frontotemporal atrophy of the brain, including the caudate, with ventricular dilation. He died 6.5 years after the onset of symptoms due to bronchopneumonia with septicemia.

A neuropathological examination revealed frontotemporal lobar atrophy with basal pronounced and leptomeningofibrosis. His brain weighed only 1130 g. There was white matter atrophy with marked ventricular dilation (Fig. 1 A, B). Upon microscopic examination of numerous brain regions, including hemispheric big slides stained by different methods for neurons, myelin, axons, inclusion bodies, glial fibers etc., the most prominent finding was a layer-dependent neuronal depletion of the cortex starting in the upper layers (Fig. 1 C–E). In the most severely involved fronto- and temporobasal regions (Fig. 1 B) the lower laminae also became involved. In Nissl and silver stains Pick cells and Pick bodies were absent. The striatum and the nucleus lentiformis were also severely atrophic (Fig. 1 A, B) and depleted of neurons.

Cortical and subcortical astrocytosis and fibrillary gliosis were not only found in the frontotemporal region, but subcortical fibrillary gliosis was also present in the white matter of the occipital lobe, although no neuronal (Fig. 1 C) deficits could be demonstrated in the related cortex (anisomorphic gliosis).

Spongiosis was mostly found in the upper cortical layers (III, II). However, in the fronto- and temporobasal regions, and in the insula, the deep layers were also involved (Fig. 1 F).

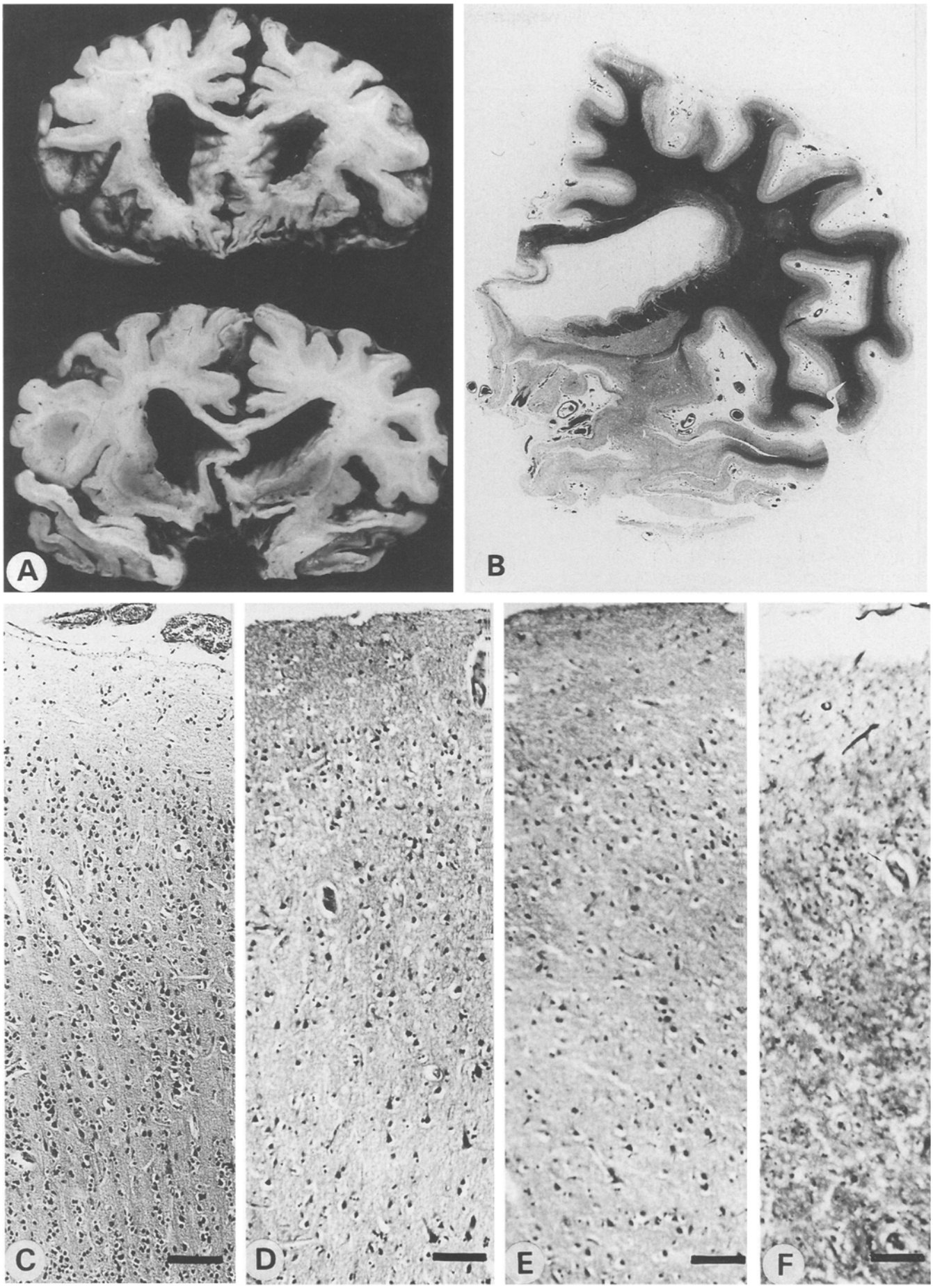
Degeneration of pigmented neurons was frequent in the S. nigra and the Locus coeruleus; however, no Lewy bodies were found. (Immunocytochemical reactions yielded poor results obviuosly due to the long formalin fixation of the brain for several months in and outside hospital).

Five further cases of mild-to-moderate FLD with progressive dementia, two of them including motor neuron disease, have been summarized in Table 1. Case 6 has been extensively described elsewhere [36].

Discussion

The nosological classifaction of mild-to-moderate frontolobar atrophy with progressive dementia in cases such

Fig. 1 A–F Frontotemporal degeneration with basal pronouncement (**A, B**): The atrophy inlcudes the cortical gray matter, the white matter (ventricular dilation), and the basal ganglia. Note the comparatively well-preserved first temporal gyrus in **A** and **B** (**B** Klüver-Barrera staining). **C** Occipital cortex with normal laminae and columnar arrangment of neurons; no reduction in the number of neurons. **D** Upper layers of the precentral region showing a significant neuronal depletion of laminae II, III_A, and III_B, which becomes even worse in the prefrontal region (**E**). Here, laminae II and III can almost no longer be distinguished from each other, **F** Severe reduction in the number of neurons with almost complete erasure of the cortical layer arrangement, and marked spongiosis in the caudal parts of the insula Reili. (**C–E** H&E staining; **F** Bodian's silver impregnation. *Bars* in **C–F** 100 μm)


A
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C
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Table 1 Further cases of dementia in lobar atrophy (cases 2–6)

Case no. Gender Age at death	Main symptoms	Duration of illness	familial	Morphology (brain weight)
2 (F184/92) Female 40 years	Change of personality Emotional instability Spells of psychomotor excitement (screaming attacks) Marked frontal atrophy in CT scans	7 years	No	Frontal lobe atrophy (1330 g) Neuronal depletion in laminae II and III Focal spongiosis in lamina II
3 (569/92) Male 73 years	Lack of memory Disorientation Change of personallity Confabulation	1 year	No	Frontal atrophy Brain edema (1450 g) Neuronal depletion of upper neocortical laminae and of entorhinal cortex Cortical and subcortical gliosis (astrocytosis)
4 (623/76) Male 58 years	Decrease of efficiency Uncertainty Anxiety Progressive mutism Incontinence	5 years	No	Frontally pronounced atrophy (1090 g) Loss of neurons, mainly in lamina III White matter atrophy Mild spongiosis of lamina II Nigra degeneration with Lewy bodies
5 (784/79) Male 58 years	Marked change of personality Progressive musculatur atrophy with fasciculations	2 years	No	Frontally pronounced atrophy (1320 g) including the caudate Neuronal depletion of lamina III Nigra degeneration Motor neuron disease
6 (Ext 194) Male 59 years	Dementia Parkinsonism Progressive neurogenic muscular atrophy with signs of pyramidal tract involvement	14 years	Yes	Frontally pronounced atrophy (1260 g) White matter atrophy Neuronal depletion of upper cortical layers Cortical astrocytosis Focal spongiosis Neurofibrillary tangles in the allocortex and brainstem Nigra degeneration with neurofibrillary tangles Motor neuron disease

as described by Brun [6, 7], Gustafson [13, 14], Neary [26, 27], Neary et al. [28, 29], The Lund and Manchester Groups [39], and in the present paper is still a matter of debate. Despite the fact that microscopically Pick cells and bodies are missing, and that these cases do not exhibit the knife-blade atrophy of typical Pick disease, the attempt to separate them from the spectrum of Pick atrophy appears arbitrary. The answer to the question of lumping or splitting depends largely on the definition of Pick atrophy.

It has been demonstrated that even in many cases of lobar atrophy with characteristic clinical symptoms and the knife-blade atrophy of typical Pick disease, Pick cells and bodies may be missing ("atypical Pick disease" [8]) [17, 18, 20]. The former have been shown to occur in about only one-third of cases; the latter in half or less of cases with the typical gross morphology of Pick atrophy (typical Pick disease [8, 18, 21]). This means that they cannot be regarded as reliable hallmarks of Pick atrophy, and thus cannot be used as inclusion cirteria for its morphological diagnosis as implied by the Lund and Manchester groups [39]. Furthermore, knife-blade atrophy also cannot be regarded as an inevitable criterion of Pick atrophy, because otherwise typical cases with mild or moderate lobar atrophy have been described [18, 21, 37].

Former investigators [5, 18, 21, 37] stressed that layer-dependent neuronal degeneration was a much more constant histological feature of Pick atrophy than the inflated neurons and argentophilic cytoplasmic inclusion bodies. The neuronal loss usually follows a certain sequential pattern starting in laminae I [18] and III_A, then progressiving via III_B to II, then to III_C and only later, if ever, to the deeper layers V to VII [21]. Other sequences, e.g., degeneration starting in the deeper layers, have also been described [21]; however, they seem to be exceptional. Jakob [18] found involvement of lamina IV only in cases with a very long clinical course. Together with the lobar distribution of the atrophy, including the striatum, cortical and subcortical fibrillary gliosis, spongiosis, and white matter atrophy, the layer-dependent neuronal degeneration has been demonstrated to be the most characteristic micromorphological feature of Pick atrophy [18, 21]. Altogether, the aforementioned features are more constant than inflated cells and inclusion bodies.

Neuronal loss, spongiosis of the upper layers, and gliosis were also described as the most prominent histological features in FLD [6, 7, 39]. In his review Brun [7] stressed that the neuronal degeneration of superficial cortical layers was the salient feature of FLD of non-Alzheimer type.

Table 2 Morphological grading of Pick atrophy

Mildly atrophic gyri	Neuronal changes in upper cortical layers	Thickening of membrana limitans gliae
Moderately atrophic gyri	Marked neuronal depletion in lower cortical layers	Increased content of glial fibers in cortex
Markedly atrophic gyri	Severe neuronal drop-out in upper and mild depletion in lower layers	Marked fibrillary gliosis of all cortical layers
Devastated gyri	Severe neuronal depletion of all cortical layers	Spongiosis of upper cortical layers

From Ref. 37

This was also included in the consensus statement of The Lund and Manchester Groups [39].

In all our cases a similar layer-dependence of the neuronal depletion centered on the superficial laminae could be demonstrated. Case 1 was a typical fronto-temporobasal type of lobar degeneration without Pick cells and bodies (see also Ref. 17).

Subcortical gliosis, which in some cases seems to be anisomorphic, indicating primary white matter involvement, was also found in one of our cases.

The aforementioned features favor a classification of such cases with the Pick spectrum according to Schneider [37], who suggested four grades of severity of the morphological changes in Pick atrophy (Table 2). The cases described by Brun [6, 7], Gustafson [13, 14], Neary [26, 27], and Neary et al [28, 29], and our cases 2–5, correspond morphologically to Schneider's grades 1 and 2, whereas case 1 matches grade 3 (Pick atrophy without Pick cells and bodies). Case 6 differs from the other cases with regard to both a familial trait for similar neurological disorders and its close similarities with the ALS-Parkinsonims-Dementia complex in Guam [15, 16]. There were even very few chromatolytic neurons, resembling Pick cells without Pick bodies [36].

Genetic studies by Lynch et al. [22] in seven members of a similar family with autosomal dominant inherited frontal lobe dementia, parkinsonism, and amyotrophy revealed a linkage to chromosome 17. Brun [6] and Gustafson [13, 14] reported positive heredity in more than 50% of their FLD cases.

By means of thorough morphometric investigations of FTD cases, Mann and South [23] could not find a difference between cases with or without Pick cells and Pick bodies. Gustafson [13] stressed that "... there were only small and non-systematic clinical differences between... FLD and Pick cases" and emphasized the "similarity between them" [13, 14].

Of 16 cases of non-Alzheimer-type dementia described by Bergmann et al. [3], 4 were labeled as classical Pick and 12 as FLD cases, 4 of them with motor neuron disease. With conventional staining the authors could not demonstrate Pick cells or bodies. However, immunohistochemical reactions with an antibody against Ubiquitin (Ub) revealed Ub-positive and tau-negative neuronal cytoplasmic inclusion bodies in 9 cases either in the cortex or in the motor nuclei.

In some cases of frontolobar atrophy the subcortical gliosis may dominate the microscopic picture in a way

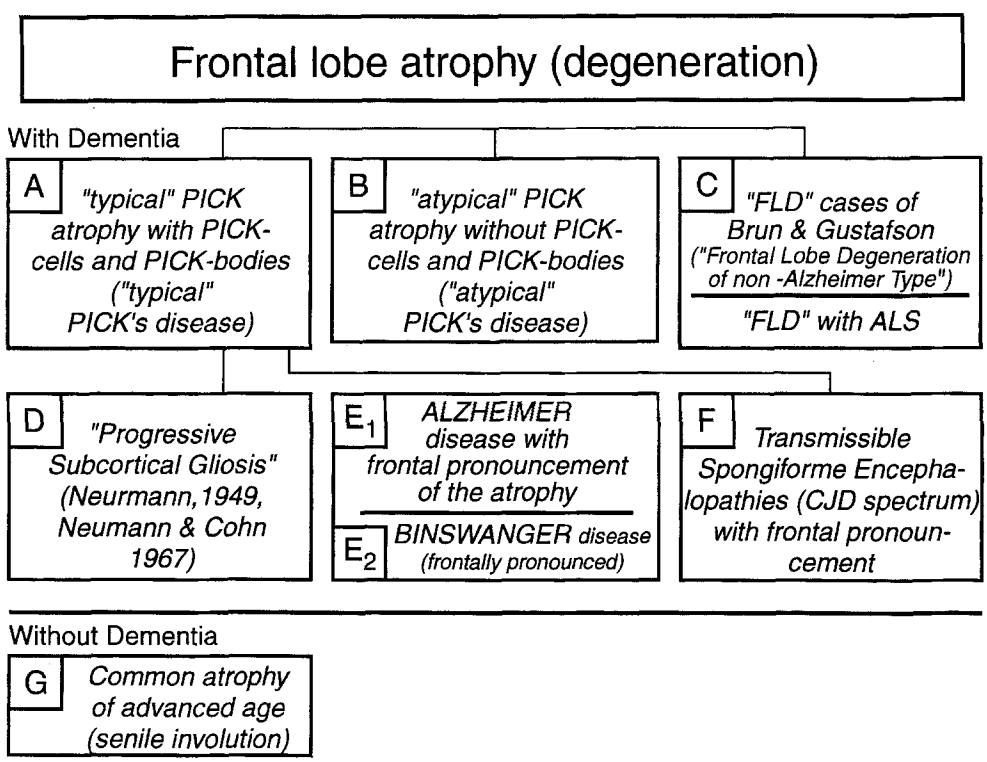

Fig. 2 A–F Main conditions under which frontal lobe atrophy or FLD may occur. **A–D** may form a common nosological spectrum with certain variations of the manifestation of the disease (Pick spectrum). Combinations of or transitional forms between **A** and **F** have been described so that there may also be a relation between **A, B** and **F**. The spongiform changes in **A** and **B** are usually marked

that such cases have been named progressive subcortical gliosis (PSG) [30, 31, 38]. In PSG cortical changes are either mild or missing [30, 31]. Included in the Pick spectrum PSG may represent one and typical knife-blade atrophy with Pick cells and bodies the other end of a spectrum that also includes severe lobar atrophy without Pick cells and bodies (present case 1) and FLD of non-Alzheimer type.

Atrophy of the frontal lobe alone is an unspecific morphological feature, wich may occur not only in cases included in the aforementioned spectrum [10, 11], but under various conditions with and without dementia (Fig. 2). In the Pick type of frontolobar atrophy the layer-dependent neuronal depletion pattern with spongiosis and subcortical gliosis, and sometimes Pick cells and bodies, are the characteristic micromorphological features that justify creating a separate taxonomic group for those cases.

However, we cannot see a convincing reason for a separate category to be introduced for those cases with mild frontal or frontotemporal atrophy and many clinical and pathological features in common with Pick atrophy. As long as the etiology of the latter remains as unknown as the cause of Brun and Gustafson's FLD of non-Alzheimer type, and we still have to follow clinical and morphological criteria for classification [39], FLD cases can be sufficiently classified with the Pick spectrum as grade 1 or grade 2 in terms of Schneider [37], the layer-dependent neuronal degeneration being the most characteristic histological feature.

However, pathology alone cannot finally resolve the problem of the true nature of the Pick spectrum of lobar atrophy, because morphological similarities do not necessarily implicate etiological homogeneity. It is more likely that the etiology of the Pick spectrum is heterogeneous, because there are, at least, familial and sporadic occurences as in Alzheimer's disease. Even the familial forms of the latter have been shown to be genetically heterogeneous [4]. Genetic analyses in the familial cases of lobar atrophy, such as those performed by Lynch et al. [22], and molecular biological approach may in the future provide further clues to the question of what should be "lumped" and what should be "split". However, until this has been done the classical designation "lobar atrophy" (i.e., Pick atrophy) with its different types (frontal, temporal, parietal, mixed frontotemporal, basal, convexity, symmetrical, asymmetrical [21]) appears to be sufficient to summarize all cases of primary circumscribed (focal) degeneration of the brain, including those with frontal or frontotemporal predominance under a general heading.

What Arnold Pick described was the lobar type of brain atrophy, including frontal, temporal, and parietal manifestations [34, 35], but neither knife-blade atrophy nor inflated neurons and inlcusion bodies, which were added later by others (see Ref. 21). Thus, referring to Pick's type of brain atrophy means to refer to primary degenerative lobar atrophy involving the white matter [35]. Therefore, it seems inadequate to "consider the Pick's type of change as ... variant of frontotemporal atrophy" [39], instead of regarding FLD as a variant of Pick's lobar atrophy [5, 18, 21, 37], the FTA cases [39] corresponding to the mild or moderate forms of the latter [37].

References

1. Bagh K von (1941) Über anatomische Befunde bei 30 Fällen von umschriebener Atrophie der Großhirnrinde (Picksche Krankheit) Vorl Mitt Arch Psychiatr 114:68–70
2. Becker E (1935) Klinische und anatomische Beiträge zur Pickschen Krankheit. Mschr Psychiatr 92:107–121
3. Bergmann M, Kuchelmeister K, Gullotta F, Schmidt KW, Gerhard L, Schröder R (1994) Different variants of non-Alzheimer degenerative dementia: a morphological study. Clin Neuropathol 13:235
4. Boller F, Forette F, Khachaturian Z, Poncet M, Christen Y (1992) Heterogeneity of Alzheimer's disease. In: Christen Y (ed) Research and perspectives in Alzheimer's disease. Springer, Berlin Heidelberg New York
5. Braunmühl A von (1930) Picksche Krankheit. In: Bumke O, Spielmeyer W (eds) Handbuch der Geisteskrankheiten, Bd XI, Teil VII, Die Anatomie der Psychosen. Springer, Berlin Heidelberg New York, pp 673–715
6. Brun A (1987) Frontal lobe degeneration of non-Alzheimer type. I. Neuropathology. Arch Gerontol Geriatr 6:193–208
7. Brun A (1993) Frontal lobe degeneration of non-Alzheimer type revisited. Dementia 4:126–131
8. Constantinidis J, Richard J, Tissot R (1974) Pick's disease: histological and clinical correlations. Eur Neurol 11:208–217
9. Filley CM, Kleinschmidt-DeMasters BK, Gross KF (1994) Non-Alzheimer fronto-temporal degenerative dementia. Clin Neuropathol 13:109–116
10. Förstl H, Baldwin B (1994) Pick und die fokalen Hirnatrophien. Fortschr Neurol Psychiatr 62:345–355
11. Förstl H, Hentschel F, Besthorn C, Geiger-Kabisch C, Sattel H, Schreiter-Gasser U, Bayerl JR, Schmitz F, Schmitt HP (1994) Frontal und temporal beginnende Hirnatrophie. Nervenarzt 65:611–618
12. Gans A (1992) Betrachtungen über Art und Ausbreitung des krankhaften Prozesses in einem Fall von Pickscher Atrophie des Stirnhirns. Z Ges Neurol Psychiatr 80:10–28
13. Gustafson L (1987) Frontal lobe degeneration of non-Alzheimer type. II. Clinical picture and differential diagnosis. Arch Gerontol Geriatr 6:209–223
14. Gustafson L (1993) Clinical picture of frontal lobe degeneration of non-Alzheimer type. Dementia 4:143–148
15. Hirano A, Kurland LT, Krooth RS, Lessell S (1961a) Parkinsonism-dementia complex, an endemic disease on the island of Guam. I. Clinical features. Brain 84:642–661
16. Hirano A, Malamud N, Kurland LT (1961b) Parkinsonism-dementia complex, an endemic disease on the island of Guam. II. Pathological features. Brain 84:662–679
17. Hulette CM, Crain BJ (1992) Lobar atrophy without Pick bodies. Clin Neuropathol 11:151–157
18. Jakob H (1979) Die Picksche Krankheit. In: Hippius H, Janzarik W, Müller C (eds) Monographien aus dem Gesamtgebiete der Psychiatrie, Bd 23, Springer, Berlin Heidelberg New York
19. Jellinger K, Bancher C (1994) Incidence of non-Alzheimer dementia in large consecutive autopsy series. Clin Neuropathol 13:254
20. Knopman DS, Mastri AR, Frey WH, Sung JH, Rustan T (1990) Dementia lacking distinctive histologic features: a common non-Alzheimer degenerative dementia. Neurology 40:251–256
21. Lüers Th, Spatz H (1957) Picksche Krankheit. In: Lubarsch O, Henke F, Rössle R, Scholz W (eds) Handbuch der speziellen pathologischen Anatomie und Histologie, Bd XIII/1A Springer Berlin Heidelberg New York, pp 614–715
22. Lynch T, Sano M, Marder KS, Bell KL, Foster NL, Defendini RF, Sima AAF, Keohane C, Nygaard TG, Falm S, Mayeux R, Rowland RL, Wilhelmsen KC (1994) Clinical characteristics of a family with chromosome 17-linked disinhibition-dementia-parkinsonism-amyotrophy complex. Neurology 44:1878–1884

23. Mann DM, South PW (1993) The topographic distribution of brain atrophy in frontal lobe dementia. Acta Neuropathol 85: 334–340
24. Mesulam M-M (1982) Slowly progressive aphasia without generalized dementia. Ann Neurol 11:592–598
25. Minauf M, Jellinger K (1969) Kombination von Amyotrophischer Lateralsklerose mit Pickscher Krankheit. Arch Psychiatr Nervenkrankh 212:279–288
26. Neary D (1990) Dementia of frontal lobe type. J Am Geriat Soc 38:71–72
27. Neary C (1991) Non-Alzheimer's disease forms of cerebral atrophy. J Neurol Neurosurg Psychiatry 53:929–931
28. Neary D, Snowden JS, Northen B, Goulding P (1988) Dementia of frontal lobe type. J Neurol Neurosurg Psychiatry 51: 353–361
29. Neary D, Snowden JS, Mann DMA, Northen B, Goulding P, Macdermott N (1990) Frontal lobe dementia and motor neuron disease. J Neurol Neurosurg Psychiatry 53:23–32
30. Neumann MA (1949) Pick's disease. J Neuropathol Exp Neurol 8:255–282
31. Neumann MA, Cohn R (1967) Progressive subcortical gliosis. A rare form of presenile dementia. Brain 90:405–418
32. Pick A (1892) Über die Beziehungen der senilen Hirnatrophie zur Aphasie. Prager Med Wschr 17:165–167
33. Pick A (1901) Senile Hirnatrophie als Grundlage von Herderscheinungen. Wien Klin Wschr 14:403–404
34. Pick A (1904) Zur Symptomatologie der linksseitigen Schläfenlappenatrophie. Mschr Psychiatr Neurol 16:378–388
35. Pick A (1906) Über einen weiteren Symptomenkomplex im Rahmen der Dementia senilis, bedingt durch umschriebene stärkere Hirnatrophie (gemischte Apraxie). Mschr Psychiatr Neurol 19:97–108
36. Schmitt HP, Emser W, Heimes Ch (1984) Familial occurrence of amyotrophic lateral sclerosis, parkinsonism, and dementia. Ann Neurol 16:642–648
37. Schneider C (1927) Über Picksche Krankheit. Mschr Psychiatr 65:230–275
38. Seitelberger F (1968) Allgemeine Neuropathologie der Alterns- und Aufbrauchskrankheiten des Gehirns. Verh Dtsch Ges Pathol 52:32–61
39. Lund and Manchester Groups (1994) Clinical and neuropathological criteria for frontotemporal dementia. J Neurol Neurosurg Psychiatry 57:416–418
40. Wechsler AF, Vesity MA, Rosenschein S, Fried J, Scheibel AB (1982) Pick's disease: a clinical computed tomographic and histologic study with Golgi impregnation observations. Arch Neurol 39:287–290