CSF analysis of a subgroup of Alzheimer's disease patients presenting with focal temporal dysfunction

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BACKGROUND

Alzheimer's disease (AD) is clinically heterogeneous in its presentation and progression, demonstrating variable topographic distributions of atrophy and hypomethabolism/hypoperfusion. AD most commonly begins as an episodic and semantic memory impairment; decline in other domains (language, executive functions, visuospatial functions) emerging as disease progresses. Several authors have recently described that after amnesic mild cognitive impairment (aMCI), some of the patients who convert to AD show the classical onset of disease, whereas other show isolated deficit of episodic and semantic memory, with no impairment in the remaining cognitive domains. The latter have been considered as an atypical AD variant characterized by "focal temporal lobe dysfunction" (TLD). TLD is usually associated with later age of onset and slower rate of progression. SPECT imaging demonstrates hypoperfusion limited to the mesio-temporal lobes, while the temporal-parietal changes seen in typical AD are absent. Longitudinal studies demonstrate slow or no change in MMSE scores and even when memory is significantly impaired, visuospatial and executive functions are usually unaffected. Pathological studies have shown plaques and neurofibrillary tangles limited to the limbic regions, with little or no spread to the neocortical areas. In literature, there is a lack of studies concerning TLD and its associated CSF alterations.

AIM

The aim of this study is therefore to analyze CSF concentrations of Aβ 1-42 amyloid (Aβ 1-42), phosphorylated-Tau (p-Tau) and total-Tau (t-Tau) in this subset of patients and compare them with typical AD to assess differences.

METHODS

We evaluated CSF biomarkers of 8 patients with neuropsychological evidence of a selective temporal impairment (TLD) with mean mini mental state examination (MMSE) score 21/30 and mean age 79.5 years and compared them with 8 patients with typical AD (mean MMSE score 18,5/30 - mean age 79,5 years) (Tab. 1).

RESULTS

Our results show in TLD group a mean Aβ 1-42 258,1 pg/ml, t-Tau 862,5 pg/ml and p-Tau 124,0 pg/ml. Typical AD group show a mean Aβ 1-42 246,0 pg/ml, t-Tau 392,1 pg/ml and p-Tau 74,6 pg/ml (Tab. 2). Both show a profile compatible with diagnosis of AD but with significant high levels of t-Tau in TLD group vs typical AD group (Fig.1).

	TLD	Typical AD
Mean Age	79,5	79,5
MMSE	21	18,5
Rey R.I.	25	20,75
Rey R.D.	1,5	1
Fig. Rey Copia	32,3	16,94
Figura Rey R. D.	9,5	4,5
Matrici di Raven	23,5	19,75
F.V.F.	20	16

Tab. 1. *Neuropsychological evaluation*

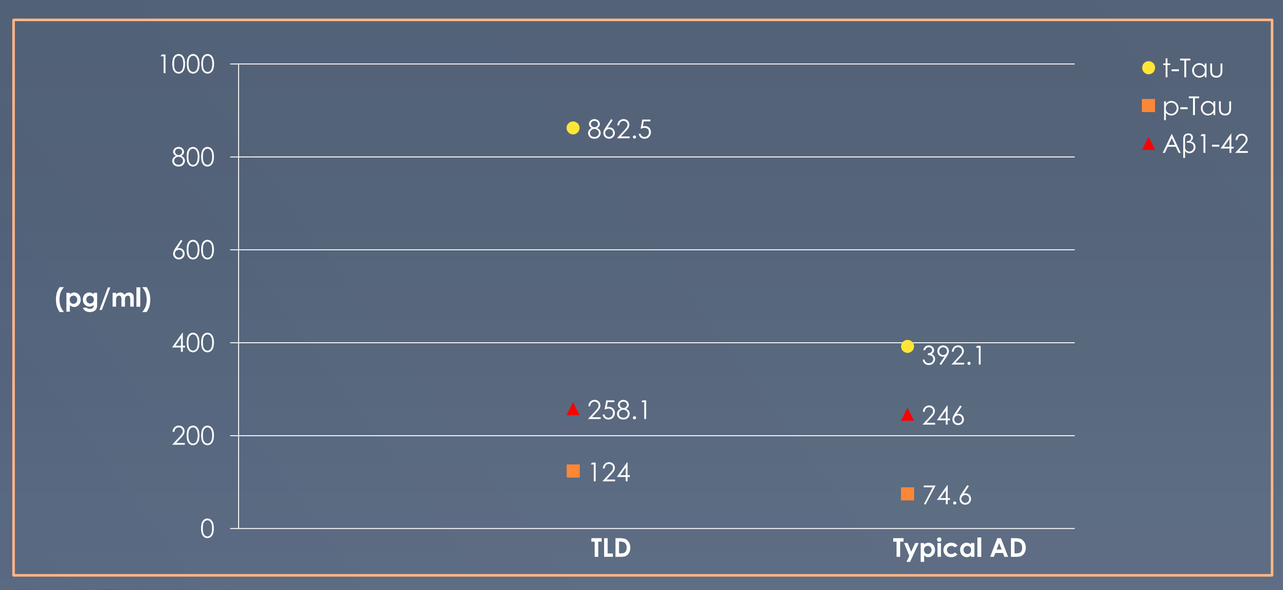

Fig. 1. *CSF biomarkers distinct by groups*

	TLD	*Typical AD*	*p*
t-Tau (pg/ml)	862,5	392,1	0,004
p-Tau (pg/ml)	124,0	74,6	NS
Aβ1-42 (pg/ml)	258,1	246,0	NS

Tab. 2. *CSF biomarkers*

CONCLUSIONS

Since higher levels of t-Tau relate to a faster rate of progression, we suggest that t-Tau could be related with focal dysfunction rather than widespread. Further investigation is however needed to understand why a typical AD-CSF pattern, generally implying an aggressive neuronal degeneration, in this case is associated with such a slow progression of disease.

References:

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