PostScript

Relationship between asthma severity and progression of Alzheimer's disease

Severity of asthma is occasionally modulated by neuropsychiatric conditions.[1] However, little is known about the impact of cognitive decline on asthma severity. Cognitive decline is a core symptom in patients with Alzheimer's disease (AD).[2] AD is a disease characterised by progressive cholinergic failure[3] that could possibly reduce airway hyperresponsiveness to cholinergic stimulation and thus symptoms of asthma. Furthermore, the functions of T lymphocytes—which play a crucial role in the development of chronic asthma—are partially impaired in patients with AD related diseases.[4] We hypothesised that declining cognitive function might result in an improvement in asthma, and prospectively studied the contribution of the progression of AD to the clinical course of asthma.

Eight patients with asthma of mean (SE) duration 15.3 (0.9) years with concomitant AD were identified and prospectively followed for 5 years from 1995 to 2000. All subjects were treated with oral theophylline (200 mg twice daily) and a 200 μg dose of fenoterol given by a flow driven inhaler as needed. Family members of the patients completed a diary card that recorded asthma symptoms,[5] use of daily medication, and the number of hospital admissions for asthma during the 5 years prior to study entry and the 5 year observation period. Cognitive function was assessed by Mini-Mental State Examination (MMSE)[6] and sputum eosinophil counts[7] and methacholine challenge tests[8] were performed both at enrolment in the study and at the end. Informed consent was obtained from each patient, his or her family, and an attending physician.

MMSE scores were significantly decreased during the 5 year observation period in all subjects (table 1). Overall attack frequency and severity of asthma symptoms significantly decreased during the progression of cognitive impairment in all but one asthmatic subject with AD (table 1). Induced sputum obtained at the end of the study from seven subjects with improved asthma had a significantly lower percentage of eosinophils than at the start of the study (2.2 (0.4)% at end point *v* 10.7 (2.8)% at baseline, n=7, p=0.008), but there were no significant differences in the mean percentages of macrophages, neutrophils, or lymphocytes. By contrast, in all subjects the minimum cumulative dose of methacholine that induced an increase in respiratory resistance at the end of the study was not significantly different from that obtained at study enrolment (0.426 (0.252) U at end point *v* 0.368 (0.144) U at enrolment in the study, n=8, p=0.26). No other precipitating factors for asthma were identified during the study period in any subject.

Both overall attack frequency and severity of asthma symptoms decreased significantly during the progression of cognitive impairment in asthma patients with AD. However, peripheral cholinergic function might not be impaired in the airway in patients with AD despite an extensive loss of central cholinergic neurons.[3] It has been reported that the nervous system may modulate immunological and inflammatory responses.[9] Our results suggest that progression of AD might provide an ameliorating effect on the clinical course of asthma, probably due to alterations in the immunological responses including eosinophilic inflammation in the airway.

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IL-1 haplotypes and lung function decline

We read with interest the paper by Joos *et al*[1] on the association of IL-1 gene haplotypes with decline in lung function in smokers and share their view on a possible role of IL-1 genetics in inflammatory respiratory diseases. We have analysed the same polymorphism by

Table 1 Assessment of asthma severity and change in cognitive function at study entry (baseline) and 5 year follow up (end point) in asthma patients with Alzheimer's disease

			MMSE score		Asthma symptom score		Daily inhaler puffs		Number of hospital admissions for asthma	
Case	Age (y)	Sex	Baseline	End point	Baseline	End point	Baseline	End point	Baseline	End point
1	67	M	23	18	6.4	1.2	1.3	0	2	0
2	66	M	21	16	8.6	2.2	1.4	0	2	0
3	70	F	23	17	10.2	1.6	2.4	0	3	1
4	65	M	22	15	7.8	1.2	2.6	1.4	3	0
5	65	F	21	16	7.5	0.4	3.3	1	2	0
6	69	F	23	17	9.4	3.6	1.9	0.4	3	0
7	66	F	22	16	9.2	2.4	2.2	0	2	0
8	68	M	23	21	7.6	7.4	2.8	2.6	3	2
Mean (SE)	67.0 (0.7)		22.3 (0.3)	17.0 (0.7)*	8.4 (0.5)	1.8 (0.4)†	2.2 (0.3)	0.4 (0.2)‡	2.4 (0.2)	0.1 (0.1)§

MMSE=Mini-Mental State Examination; SE=standard error.
*p<0.0001 (Wilcoxon rank test) compared with baseline data in all asthma patients with Alzheimer's disease; †p<0.0001; ‡p=0.0001; §p<0.0001 compared with baseline data in seven asthma patients with Alzheimer's disease (cases 1–7).