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LETTER TO THE EDITORS

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Propionibacterium acnes in the cortex of patients with Alzheimer's disease

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Abstract *Propionibacterium acnes* was found in the cortex of three patients with Alzheimer's disease and in one frontal cortex of an elderly patient with cardiovascular risk factors and hypoxia due to a large glioblastoma of the right frontal lobe with severely increased intracranial pressure. *Propionibacterium acnes* is an atypical anaerobic bacterium which is sensitive to cephalosporins, but insensitive to metronidazole. It is concluded that a capillary microangiopathy (in consequence of old age and cardiovascular risk factors such as high blood pressure) leads to cortical hypoxia and reduced resistance of the cortical immune system. Prevention by dietary regimes counteracting microangiopathy and treatment with cephalosporins are recommended.

Key words Alzheimer's dementia · *Propionibacterium acnes* · Anaerobic infection · Microangiopathy · Vascular risk factors · Dietary prevention · Cephalosporins

Introduction

There are signs of inflammation in the cortex of patients with Alzheimer's disease [4, 16], and microorganisms have been found post mortem in the brains [10]. Their nature could not be positively identified post mortem; actinomyces were suspected. We therefore carried out cortical biopsy in four patients with typical Alzheimer's disease (with informed consent of the patients and their relatives) and in five controls (patients with a cerebral tumor).

Results

There was no growth of microorganisms in aerobic cultures. In three cases of Alzheimer's disease, however, *Propionibacterium acnes* was identified in anaerobic cultures both by microbiological methods as well as gas chromatography; no actinomyces were found. In the fourth patient there was no growth of any microorganisms, probably because this patient received an injection of cephalosporin by mistake from a well-meaning anesthesiologist – a routine before cerebral operations which was intentionally omitted in the other Alzheimer's and control cases. In four controls (cortical tissue from patients with a cerebral tumor) all cultures resulted in no growth of any microorganisms. In the fifth control, however, *Propionibacterium acnes* was found. This patient, a 69-year-old man, had a severely increased intracranial pressure (with ataxia and disorientation) due to a large glioblastoma of the right frontal lobe with numerous hemorrhages into the mass. Furthermore, this patient had type II diabetes and hypercholesterolemia. These circumstances presumably caused hypoxia of the right frontal cortex.

Discussion

In some families Alzheimer's disease is hereditary, and several genes have been identified, but most cases are sporadic, associated with old age [9] and cerebral atrophy. The most common cause of cerebral atrophy of old age is microangiopathy. Microangiopathy may occur in all tissues. Because some neurologists believe that there is cerebral microangiopathy only in subcortical structures, we designed a quantitative method to measure signs of microangiopathy from the primary electronic data of computerized tomography. It was found that patients with stroke in consequence of macroangiopathy or embolism also have significantly more CT signs of cerebral microangiopathy at both subcortical and cortical levels than control persons of similar age [13], suggesting common risk factors for cerebral micro- and macroangiopathy as known from peripheral circulation. With magnetic resonance imaging Alzheimer patients have more signs of microangiopathy than control cases of similar age [7, 19]. There are similar data from verified cases of Alzheimer's

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dementia [1, 15]. There is capillary microangiopathy especially in the cortex of patients with Alzheimer's disease [20]. The causes of this microangiopathy are probably similar as in other cases of microangiopathy [12]: Vascular risk factors such as old age, high blood pressure and type-II diabetes (including prediabetes/hyperinsulinemia) [2, 5, 6, 17, 18]. The fact that apolipoprotein E4 [3] and lack of estrogen in postmenopausal women are risk factors for Alzheimer's disease agree with this interpretation. Apo E4 is also a risk factor for stroke, multiinfarct dementia, and cardiovascular disease.

Propionibacterium acnes is an atypical anaerobic bacterium; it is sensitive to penicilline and cephalosporin, but insensitive to metronidazole. *Propionibacterium acnes* tends to cause chronic infections, such as endophthalmitis, cerebral shunt infections or osteomyelitis, but it may also exist without causing signs of inflammation in the comedones of acne. A hypoxic state of the cortex in Alzheimer's disease is well compatible with the finding of anaerobic microorganisms. *Propionibacterium acnes* has a microscopic appearance similar to streptomyces which were suspected from post mortem findings [10], and both microorganisms have a similar skin with wax.

Living bacteria in the cortex of patients with Alzheimer's dementia are surprising in view of present ideas about the cause of this disease; most scientists may be inclined to discard this finding as an artifact due to contamination (there was recently a similar story with helicobacter pylori). However, from post mortem data there is little doubt that bacteria-like microorganisms do indeed live in the brains of these patients [10].

Why does mainly the association cortex of the frontal and temporal lobes suffer from Alzheimer's disease, although microangiopathy presumably damages the entire neocortex? This may be explained by the hypothesis that the phylogenetically youngest cortex suffers most because its capillary supply is less robust than that of the older parts of the neocortex [14]. The formation of amyloid beta protein is not specific for Alzheimer's disease; increased amounts of it have also been found in angiopathic dementia, Creutzfeldt-Jakob-disease, Gerstmann-Sträussler-Scheinker syndrome, Parkinson's disease, and aging without dementia. The microorganisms in the cortex of patients with Alzheimer's disease should also be further investigated by post mortem methods. In the meantime, however, therapeutic trials are justified using cephalosporins and for prevention dietary regimes conteracting microangiopathy. A hint is that in Japan, where cardiovascular disease is rare (due to dietary factors as generally believed) Alzheimer's disease is also less frequent than in Western countries [8, 11].

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