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Autopsy survey for Alzheimer's disease in Nigerian Africans: A preliminary report

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Summary

We carried out an autopsy survey on 198 brains of Nigerians aged 40 years and above to determine the occurrence of (neuropathognomonic) changes of Alzheimer's disease (AD) in our elderly patients. Forty five patients (23%) were above 65 years of age. Appropriately stained histological sections of various parts of the brains showed mild cortical neuronal loss and absence of neurofibrillary tangles, senile plaques and amyloid angiopathy — hallmarks of Alzheimer's disease and ageing reported in the Caucasians and Japanese.

Résumé

Nous avons effectué un étude d'autopsie sur 198 cerveaux de Nigeriens qu'avaient 40 ans et plus pour déterminer l'événement de changement (neuropathogonomique) de la démence d'Alzheimer dans nos malades d'un certain âge. Quarante-cinq malades (23%) avaient plus de 65 ans. À propos les sections tachés histologicales de plusieurs parties du cerveaux montaient une perte de neurones corticales bénin et absence des embrouillements neurofibrilaires, les plaques séniles et angiopathie amyloide — poincons de la démence d'Alzheimer et de la viellesse rapporté dans caucasiens et japonais.

Introduction

In the developed countries, the demantias of the elderly presently constitute one of the commonest disabilities afflicting some 5% to 8% of the population above the age of 65 years[1]. The prevalence ratio rises to 15% to 20% or higher in those above the age of 80 years[1,2,3]. Apart from Japan and possibly the Soviet Russia, some 50% or more of the dementias in the elderly in developed countries is caused by Alzheimer's disease (AD) [5-8]. Dementias of the elderly including AD has been reported in the Chinese in China[9,10]. However, in Africa, as in most other developing parts of the world, there is little or no reliable information on the disease. For example, no single authentic case of AD has been reported in an indigenous Black African. In one community-based study in Nigeria involving a door-to-door survey of nearly 19000 subjects, 6% of whom were over the age of 65 years, no patient with dementia was encountered[11]. Yet the prevalence of AD in Black Americans (who are predominantly of West African lineage) does not differ markedly from that of American Caucasians[12-14].

We therefore carried out an autopsy survey to find out if the key neurohistological hallmarks of AD, reported in a lesser degree in ageing Caucasians and Japanese[14-23], occur in Nigerian subjects aged 40 years and over so as to forecast the emergence of the disease.

Materials and methods

The material for the autopsy survey comprised brains of consecutive 198 Nigerians aged 40 years and above who died in 1986 and 1987 in the University College Hospital, Ibadan (Nigeria's first and premier leading teaching hospital as well as the National Centre of Excellence in Clinical Neurosciences) and in whom autopsy was done. None of the subjects was known to suffer from a dementing illness. The corpses were put in refrigerated columns within one hour of death and the brains which were removed within 24 hours of death were fixed in neutral 20% formalin for at least two weeks. For Nigerians who had no recorded birthdates, ages were accurately assessed to the nearest half a decade by using historical data such as the one compiled by Ajayi and Igun[24] for the 1963 census of Nigeria, an approach frequently used in epidemiological surveys in Nigeria[25].

* Presented in part (by B.O. Osuntokun) at the 14th World Congress of Neurology, New Delhi, India, October 22-27, 1989.

Sections were taken from the frontal, temporal, parietal and the occipital lobes as well as from the hippocampus, entorhinal cortex, amygdala, corpus striatum and the brain stem at the levels of the superior and inferior colliculi. Blocks were embedded in paraffin wax and cut at section thickness of 5 to 10 micrometers. Microscopic sections were processed and stained with haematoxylin and eosin, congo red, phosphotungstic acid haematoxylin, luxol fast blue and modified Bielschowsky silver impregnation[6]. It was well appreciated that variations in the staining conditions, especially of the silver stain could affect the sensitivity of the results and such variations were carefully avoided. Each histopathologic section was diligently searched under high and low power microscope lens for histological hallmark features of AD[27] i.e. the presence of senile plaques, neurofibrillary tangles and amyloid vascular degeneration. In sections of the hippocampus, granulovacuolar bodies (intraneuronal inclusion bodies) and Hirano bodies (elongated eosinophilic structures) were looked for in addition.

Following the results of the initial examination, no attempt was made to obtain any quantitative or even semi-quantitative data in the absence of tangles and plaques. The neurohistological techniques and interpretation were cross-checked by (T.A.J.) with those of a well established neuropathology laboratory in the United Kingdom at the Institute of Psychiatry, London, during a two week visit and who (T.A.J.) also established that the techniques detected tangles and plaques in control brain tissues.

Results

Table 1 shows the age and sex distribution of the patients surveyed at autopsy. There was a slight male preponderance and 45 (23%) of them were over the age of 65 years. None of the brains showed neurohistological hallmarks of AD such as tangles and plaques. Mild cortical neuronal loss was however present in many. Professor Colin Masters of Department of Pathology, University of Melbourne, Victoria, Australia, kindly offered to carry out immunoperoxidase staining with formic acid treatment[20] for beta A4 amyloid on paraffin blocks of brain sections including the frontal and hippocampal cortex (sent by air from Ibadan to Melbourne through special delivery services of D.H.L. Ltd) of some of the subjects. Ten of eleven subjects including four patients over the age of 65 years (two females aged 67 and 70 and two males each aged 70 years) showed no beta A4 amyloid positivity. However in one case, that of a 55 year old male there were a few amorphous beta A4 amyloid positive cortical plaques, but the "changes were of a mild degree and insufficient for the diagnosis of Alzheimer's disease".

Table 1: Age and sex distribution of the patients surveyed

Age Range (years)	Males	Females	Total(%)
< 44	18	10	28 (14.1)
45-49	9	14	23 (11.6)
50-54	18	24	42 (21.2)
55-59	16	14	30 (15.1)
60-4	18	12	30 (15.1)
65-69	14	12	26 (13.1)
70-74	10	3	13 (6.6)
75-79	3	—	3 (1.6)
80 +	1	2	3(1.6)
Total	107	91	198 (100)

Discussion

We are suprised by the results of this autopsy survey which suggest that histological hallmarks of AD are rare or currently absent in the Nigerian community studied. If the prevalence ratios of AD for the developed countries hold for Nigerians, about two of the 45 brains of the patients above the age of 65 years surveyed at autopsy should show neuropathological features of AD lesions but none showed such features. It has been pointed out that an epidemiological approach which circumvents the problem of reliable and valid diagnosis of AD is to work with brains rather than with persons[7] for in spite of the increasing accuracy of up to 90% of clinical and laboratory-aided diagnosis of AD[28,29], errors can still be substantial. In one study of 199 subjects (including Black Americans) who died in a teaching hospital, the frequency of plaques and neurofibrillary tangles increased monotonically after the age of 71 years[14]. Therefore our autopsy observation in the Nigerians, if confirmed in a larger series, represents a significant finding in the epidemiology of AD. The staining method we employed may not be as sensitive as others in detecting neuropathological lesions of AD for silver stains are noted for being capricious[16]. The nucleus basalis of Meynert (the magnocellular basal nucleus) the major source of cholinergic innervation of the cerebral cortex in mammals and humans and in which degeneration is almost always present in AD may appear relatively normal in silver-stained and even acetylcholinesterase-stained sections but shows neurofibrillary degeneration and neuritic plaques when stained by thioflavine methods[30]. Beta A4 amyloid and senile plaques were found in the brain of one Nigerian subject aged 55 years. Further studies would aim at using immunocytochemical methods[20,21] to delineate the frequency of occurrence of histological hallmarks of AD and AD lesions in Nigerians. Nevertheless compared with Caucasian and Japanese it would appear that these changes are currently rare in Nigerian subjects, for among the former 25% to 80% of normal undemented persons over the age of 60 had plaques and or tangles at autopsy. Although even aged rhesus monkeys show amyloid deposits in plaques and around blood vessels in the brain[31,32], it is possible that the paucity of AD lesions in brains of elderly in some communities such as the Nigerian studied may be due to biological variation (e.g. a survival elite sequel to high childhood mortality) or absence of putative as yet unknown environmental aetiological factors or the presence of some protective factor(s). It is relevant to our finding that in one report from Baltimore, USA, histological hallmarks of AD were significantly less common in brains of undemented White Americans ($p = 0.01$) [33]. The Black Americans are of the same stock as the Nigerians i.e. West African negro. We have just completed a community-based door-to-door survey for dementia involving 292 elderly (> 65 years) Nigerians: no subject suffered clinically from AD as defined by DSM-III-R and NINCDS-ADRDA[29,34] (Ogunniyi, Osuntokun, Lekwawa, Falope, in preparation). The autopsy survey we describe is continuing and it is being planned to compare blind, the neuropathology of the brain of elderly Nigerians with those of American Blacks and Australian Caucasians matched for age and sex.

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