J. Anat. Sciences, 24(1): June 2016, 1-6

Original Article

ALZHEIMER'S BRAIN : GROSS AND MICROSCOPIC STUDY

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ABSTRACT :

Introduction : Cortical atrophy is a common feature of many of the diseases that affect the brain. Atrophy of any tissue means a decrement in the size of the cell, which can be due to progressive loss of cytoplasmic proteins. One of the most common causes of cortical atrophy is Alzheimer's disease (AD). It is a progressive chronic neurodegenerative disorder and one of the leading causes of dementia.

Material and methods : 30 adult human brains preserved in formalin were obtained for establishing cerebral asymmetry, from the Department of Anatomy, King George's Medical University UP, Lucknow. Among them, one specimen was found with severe cerebral atrophy on left side. Gross and histological study was done to compare various parts of both cerebral hemispheres.

Results : On gross examination, diffuse atrophy and cortical thinning was noted especially in the parietal, frontal and temporal lobes of left side. The cortical surface appeared smooth. The cerebral gyri were narrow and the sulci widened. Corpus callosum was merely a 1mm thin sheet on left side. The lateral and third ventricles were enlarged. Coronal sections of the brain showed atrophy, mainly restricted to the white matter. Shrinkage of hippocampus was also observed. Microscopic examination revealed neuronal loss, granulovacuolar bodies, amyloid plaques, neurofibrillary tangles and Hirano's bodies, especially in cerebral cortex and hippocampus on both sides but more obvious on left side.

Conclusion : Gross and histological features suggest that the brain is of Alzheimer's diseased patient.

Key words : Cerebral cortex, hippocampus, atrophy, amyloid plaques, neurofibrillary tangles.

INTRODUCTION

The largest part of the brain is cerebrum. It consists of two cerebral hemispheres which are partially separated from each other by a longitudinal fissure. Each cerebral hemisphere is covered by a layer of grey matter, known as cerebral cortex. The cerebral cortex is not a smooth surface but shows complicated folds termed gyri and the grooves lying in between the gyri are referred to as sulci. The formation of gyri and sulci is an attempt to increase the surface area of the cerebral cortex by increasing the number of nerve cells in grey matter for better information processing capabilities. This folding is a prominent feature of human cerebrum. In other higher animals, the cerebral surface is relatively smooth. The total surface area of cerebral cortex is 2200-2500 cm2. The cortex consists of 40% mass of the brain with an enormous number of nerve cells (about 14-16 billion).[1] The cerebral cortex plays a key role in memory, attention, perception, awareness, thought, language, and consciousness. The human cerebral cortex is 2 to 4 millimetres thick.[2]

A healthy adult human brain has about 100 billion neurons, each with long, branching extensions. These extensions enable individual neurons to form connections with other neurons. At such connections, called synapses, information flows in tiny bursts of chemicals that are released by one neuron and detected by a receiving neuron. The brain contains about 100 trillion synapses. They allow signals to travel rapidly through the brain's circuits, creating the

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cellular basis of memories, thoughts, sensations, emotions, movements and skills.

Cerebral atrophy is a common feature of many of the diseases that affect the brain. Atrophy of any tissue means a decrement in the size of the cell, which can be due to progressive loss of cytoplasmic proteins. One of the most common causes of cortical atrophy is Alzheimer's disease (AD). It is a progressive chronic neurodegenerative disorder and one of the leading causes of dementia. In brain tissue, atrophy describes a loss of neurons and the connections between them. Atrophy can be generalized, which means that all of the brain has shrunk; or it can be focal, affecting only a limited area of the brain and resulting in a decrease of the functions that area of the brain controls. If the cerebral hemispheres (the two lobes of the brain that form the cerebrum) are affected, conscious thought and voluntary processes may be impaired. Some degree of cerebral shrinkage occurs naturally with age; after the brain completes growth and attains its maximum mass at around age 25 years and it gradually loses mass with each decade of life. Brain atrophy does not affect all regions with the same intensity as shown by neuroimaging.

Hippocampus is a longitudinal elevation, located in the entire length of the floor of inferior horn of lateral ventricle.[1] In primates, it is located in the medial temporal lobe underneath the cortical surface. Hippocampal atrophy is a form of brain damage that impacts both memory and spatial navigation. It is often associated with memory-loss conditions, such as dementia and Alzheimer's disease.

The lateral ventricle is a large cavity situated in each cerebral hemisphere. Third ventricle is situated in the midline, between the right and left lateral ventricles. Ventriculomegaly can be due to atrophy of structures that surround the lateral ventricles. A decrease in the size of the surrounding periventricular structures allows the ventricles to expand and fill in the space.

MATERIAL AND METHODS

30 adult human brains preserved in formalin were obtained for establishing cerebral asymmetry, from the Department of Anatomy, King George's Medical University UP, Lucknow. Among them, one specimen was found with severe cerebral atrophy on left side. Gross and histological study was done to compare various parts of both cerebral hemispheres. Intact meninges were removed carefully from the surface of brain for better visualization of structures. The fronto-occipital length and cortical thickness of right and left cerebral hemispheres were measured using vernier calipers. After separating the two hemispheres through longitudinal fissure, antero-posterior length and depth of lateral ventricle of two sides was measured with the help of thread. The two corners of the thread were fixed by means of artery forcep and then the measured value was obtained by putting it on a measuring scale. Coronal sections were done to see the various parts in detail.

For microscopic examination, small pieces (6-7mm) of brain tissue from similar areas of atrophic parietal, frontal lobes and hippocampus was taken. Processing of tissues was done for making paraffin blocks and sections of 5 µm thicknesses were cut on a rotary microtome and stained with haematoxylin-eosin. Photographs of both gross and histological findings were taken and analyzed.

OBSERVATIONS

Macroscopic changes: On gross examination, severe diffuse atrophy and cortical thinning was noted especially in the parietal, frontal and temporal lobes of left side. The cortical surface appeared smooth. The cerebral gyri were narrow and the sulci widened. Corpus callosum was merely a 1mm thin sheet. The lateral and third ventricles were enlarged. Coronal sections of the brain showed atrophy, mainly restricted to the white matter. Shrinkage of hippocampus was also observed. Loss of brain weight was noted on left side as compared to right side (Fig. 1-4).

Fronto-occipital length and cortical thickness were decreased on left side as compared to right side while antero-posterior length and depth of lateral ventricle were increased on left side as compared to right side due to enlargement of the ventricle (Table 1).

Table I : Morphometric comparison of right and left cerebral hemisphere

Parameters	Right hemisphere	Left hemisphere
Fronto-occipital length	15 cm	14.3 cm
Cortical thickness	0.3 cm	0.1 cm
Antero-posterior length of lateral ventricle	9.8 cm	10.9 cm
Depth of lateral ventricle	1.8 cm	3.2 cm

Microscopic changes : Microscopic examination revealed neuronal loss, granulovacuolar degeneration, amyloid plaques, neurofibrillary tangles and Hirano's bodies, especially in cerebral cortex and hippocampus on both sides but more obvious on left side. Plaques appeared as fibrillary fine structure. Flame or globoid shaped structures called neurofibrillary tangles (NFTs) were also observed especially in cerebral cortex and hippocampus. Rod-shaped, crystal-like, eosinophilic intraneural structures known as Hirano's bodies (HBs) were seen in cerebral cortex and hippocampal pyramidal neurons. A large number of Granulovacuolar bodies (GVBs) appear as round vacuoles (3-4 microns) with a dense core were observed which stains blue in H&E. They were confined to the soma of hippocampal pyramidal neurons. Histological findings were noted in sections of both sides but more pronounced on left side (Fig. 5-7).

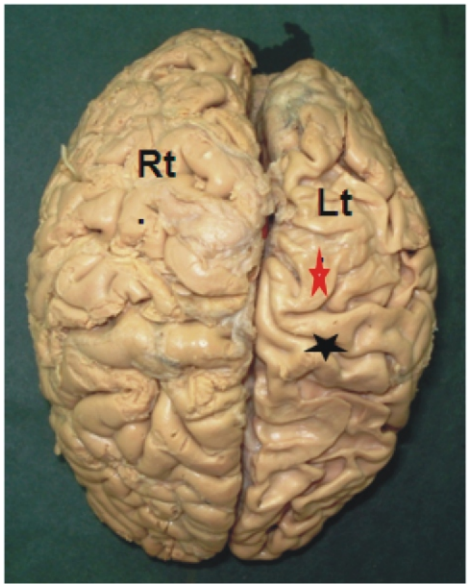

Fig. 1 : Photograph showing right and left cerebral hemisphere for difference in fronto-occipital length, narrowed gyri (red star) and widened sulci (black star) on left side.

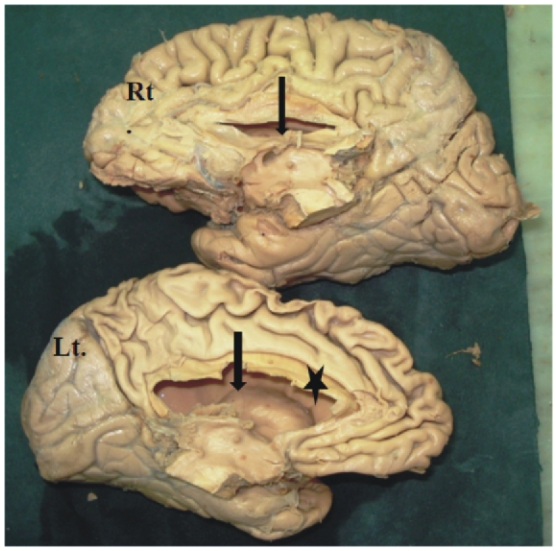

Fig. 3 : Photograph showing dilated lateral ventricle (arrow) and thinned out corpus callosum (black star).

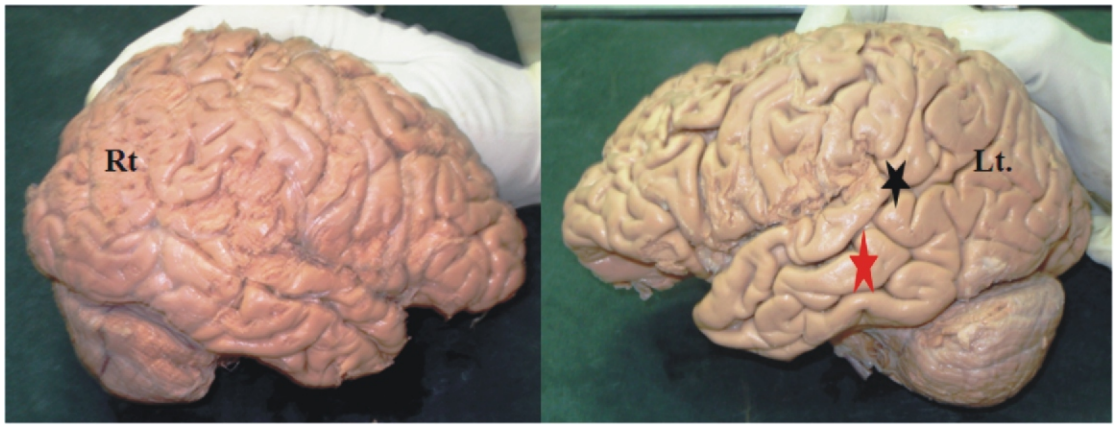

Fig. 2 : Photograph showing narrowed gyri (red star) and widened sulci (black star) in left cerebral hemisphere.

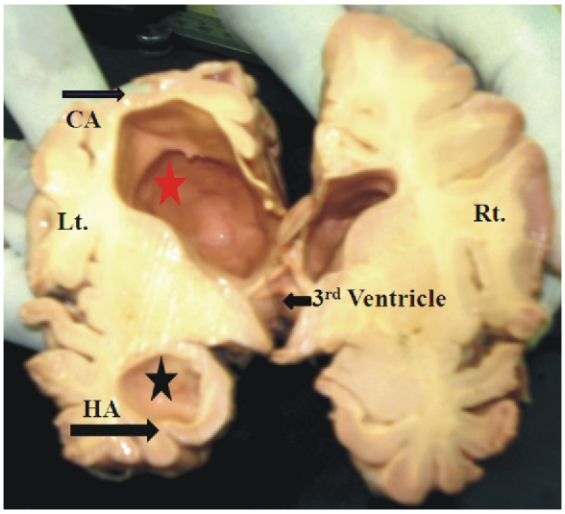

Fig. 4 : Photograph showing cortical atrophy (CA), hippocampal atrophy (HA), dilated central part (red star) & inferior horn of lateral ventricles (black star) and dilated 3rd ventricle (arrow).

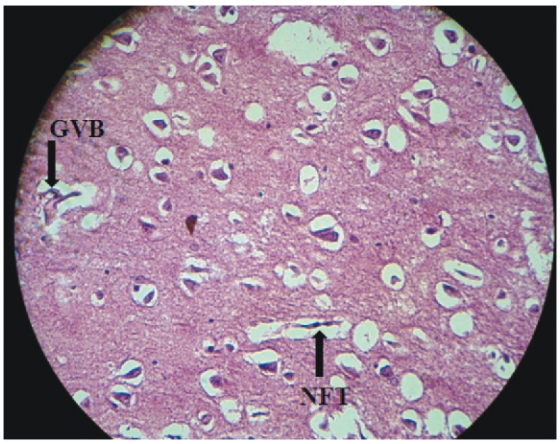

Fig. 5 : Photomicrograph of cerebral cortex showing Granulovacuolar bodies (GVB) and Neurofibrillary tangle (NFT) (HE stain; 400x).

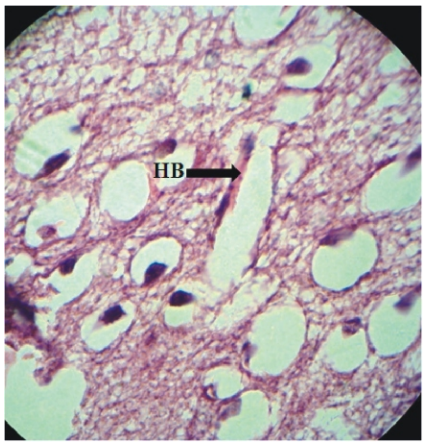

Fig. 6 : Photomicrograph of hippocampus showing Hirano's bodies (HB) (HE stain; oil immersion).

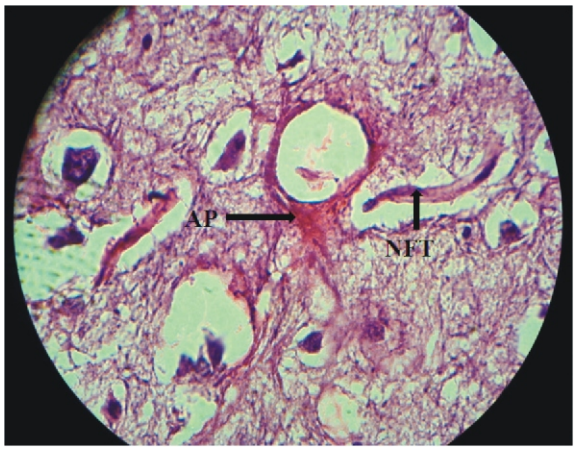

Fig. 7 : Photomicrograph of cerebral cortex showing amyloid plaque (AP) and Neurofibrillary tangle (NFT) (HE stain; oil immersion).

DISCUSSION

Brain atrophy involves the loss of neurons. Some degree of atrophy and subsequent brain shrinkage is common with old age, even in people who are cognitively healthy. However, this atrophy is accelerated in people with mild cognitive impairment and even faster in those who ultimately progress from mild cognitive impairment to Alzheimer's disease. Many factors have been implicated in affecting the rate of brain atrophy, one of which is high levels of an amino acid in the blood called homocysteine.

The genetic heritability of Alzheimer's disease (and memory components thereof), based on reviews of twin and family studies, range from 49% to 79%.(3,4) Around 0.1% of the cases are familial forms of autosomal (not sex-linked) dominant inheritance, which have an onset before age 65.[5] This form of the disease is known as early onset familial Alzheimer's disease. Most of autosomal dominant familial AD can be attributed to mutations in one of three genes: those encoding amyloid precursor protein (APP) and presenilins 1 and 2.[6] Most mutations in the APP and presenilin genes increase the production of a small protein called Aß42, which is the main component of senile plaques.[7]

AD accounts for 60% to 70% of cases of dementia. It is a chronic neurodegenerative disease that usually starts slowly and gets worse over time. The most common early symptom is difficulty in

remembering recent events (short-term memory loss).[8]

AD is characterized by loss of neurons and synapses in the cerebral cortex and certain subcortical regions. This loss results in gross atrophy of the affected regions, including degeneration in the temporal lobe and parietal lobe, and parts of the frontal cortex and cingulate gyrus.[9] Degeneration is also present in brainstem nuclei like the locus coeruleus.[10] In our study also we found profound atrophy of various regions of cerebral cortex. Studies using MRI and PET have documented reductions in the size of specific brain regions in people with AD as they progressed from mild cognitive impairment to Alzheimer's disease, and in comparison with similar images from healthy older adults.[11]

Both amyloid plaques and neurofibrillary tangles are clearly visible by microscopy in brains of those affected by AD.[12] Although many older individuals develop some plaques and tangles as a consequence of ageing, the brains of people with AD have a greater number of them in specific brain regions such as the temporal lobe.[13] They are the major pathological hallmark of Alzheimer's disease. Plaques are dense, mostly insoluble deposits of beta-amyloid peptide and cellular material outside and around neurons. In general, NFTs show a rather striking predilection to affect particular areas of the Alzheimer's diseased brains. Their density is highest in the pyramidal neurons of the medial temporal lobe (amygdala, some areas of hippocampus and subiculum) and moderate in the frontal, temporal and parietal lobe. They are aggregates of the microtubule-associated protein tau which has become hyperphosphorylated and accumulate inside the cells themselves. Crystalloid arrays of interlacing filaments displaying either a lattice-like or herringbone configuration were also noted in the cortex called Hirano's bodies. They are eosinophilic intraneural structures, most often found in the hippocampal pyramidal neurons. Granulovacuolar bodies were confined to the soma of hippocampal pyramidal neuron. The significance of HB and GVB is unknown. Lewy bodies are not rare in the brains of people with AD.[14] But we could not found Lewy bodies in our study.

Alzheimer's disease interferes with the proper functioning of neurons and synapses. In Alzheimer's disease, information transfer at synapses begins to fail, the number of synapses declines, and neurons eventually die. The accumulation of beta-amyloid is believed to interfere with the neuron-to-neuron communication at synapses and to contribute to cell death. Tau tangles block the transport of nutrients and other essential molecules in the neuron and are also believed to contribute to cell death. The brains of people with advanced Alzheimer's show dramatic shrinkage from cell loss and widespread debris from dead and dying neurons.

In Alzheimer's disease, the hippocampus is one of the first regions of the brain to suffer damage and therefore memory loss and disorientation are included among the early symptoms. Hippocampal atrophy was also noted in the present study more obvious on left side.

Dilatation of lateral and third ventricles was prominent in the present case which could be attributed to the decrease in the size of the surrounding periventricular structures thus allowing the ventricles to expand.

Advanced medical imaging with computed tomography (CT) or magnetic resonance imaging (MRI), and with single-photon emission computed tomography (SPECT) or positron emission tomography (PET) can be used to help exclude other cerebral pathology or subtypes of dementia.

CONCLUSION

In the light of present study, it can be concluded that the specimen of brain reported is of Alzheimer's disease.

REFERENCES

1. Pal, G.P. In Illustrated Textbook of Neuroanatomy, 1st ed., Lippincott Williams & Wilkins, New Delhi, Philadelphia., 2013, pp. 258, 269, 319.
2. Kandel Eric, R., Schwartz James, H., Jessell Thomas, M. Principles of Neural Science, 4th ed., United State of America: McGraw-Hill., 2000, p. 324.
3. Wilson, R.S., Barral, S., Lee, JH., et al. Heritability of different forms of memory in the Late Onset Alzheimer's Disease Family Study. J Alzheimers Dis., 2011; 23(2):249–55.

4. Gatz, M., Reynolds, C.A., Fratiglioni, L., et al. Role of genes and environments for explaining Alzheimer disease. Arch Gen Psychiatry, 2006; 63(2):168–74.
5. Blennow, K., de Leon, M.J., Zetterberg, H. Alzheimer's Disease. Lancet, 2006; 368 (9533):387–403.
6. Waring, S.C., Rosenberg, R.N. Genome-wide association studies in Alzheimer disease. Archives of Neurology, 2008; 65(3):329–34.
7. Selkoe, D.J. Translating cell biology into therapeutic advances in Alzheimer's disease. Nature, 1999; 399(6738 Suppl):A23–31.
8. Burns, A., Iliffe, S. Alzheimer's disease. BMJ (Clinical research ed.), 2009; 338: b158.
9. Wenk, G.L. Neuropathologic Changes in Alzheimer's Disease. The Journal of Clinical Psychiatry, 2003; 64 Suppl 9: 7–10.
10. Braak, H., Del Tredici, K. Where, when, and in what form does sporadic Alzheimer's disease begin? Current Opinion in Neurology, 2012; 25(Pt 6): 708–14.
11. Moan, R. MRI Software Accurately IDs Preclinical Alzheimer's Disease. Diagnostic Imaging web site. http://www.diagnosticimaging .com/mri/content/article/113619/1428344?verif y=0. Updated 20 July, 2009.
12. Tiraboschi, P., Hansen, L.A., Thal, L.J., Corey-Bloom, J. The Importance of Neuritic Plaques and Tangles to the Development and Evolution of AD. Neurology, 2004; 62(11): 1984–9.
13. Bouras, C., Hof, P.R., Giannakopoulos, P., Michel, J.P., Morrison, J.H. Regional Distribution of Neurofibrillary Tangles and Senile Plaques in the Cerebral Cortex of Elderly Patients: A Quantitative Evaluation of a One-year Autopsy Population from a Geriatric Hospital. Cerebral Cortex, 1994; 4(2): 138–50.
14. Kotzbauer, P.T., Trojanowsk, J.Q., Lee, V.M. Lewy Body Pathology in Alzheimer's Disease. Journal of Molecular Neuroscience, 2001; 17(2): 225–32.