

CASE REPORT

ALZHEIMER'S MEDICAL CONSIDERATIONS

ANTONELA CHEȘCĂ¹, SORINA ANAMARIA CHEȘCĂ², TIM SANDLE³, DMITRIY BABENKO⁴,
ILYA AZIZOV⁴

¹Faculty of Medicine, "Transilvania" University of Brașov, Romania

²Psychiatry and Neurology Hospital Brașov, Romania

³BPL, United Kingdom

⁴Karaganda State Medical University, Kazakhstan

SUMMARY

Introduction: Alzheimer's disease is a common pathology of the modern world, especially with ageing populations. This is due to both hereditary components and as a result of numerous injuries to neuronal structures and components of the central nervous system. Therefore, research from multiple perspectives is necessary to discern the complex mechanisms that give rise to this neurodegenerative disease. One perspective is with the use of imaging, and this paper illustrates the usefulness of this approach. **Methodology:** The material presented in this paper addresses the issues of the etiology of Alzheimer's disease and its effects on nerve cells and changes to the central nervous system. In order to illustrate this, information relating to patients, in the form of CT images, are detailed.

Results: From an analysis of the imaging tests presented in this paper, it is noted that the changes occur on the structures of the central nervous system: brain, cerebella cortical brain sharp, periventricular white matter. Beside specific changes, CT exam shows other structures, such as paranasal sinuses, mastoid cells or orbits, do undergo change. Differentiating between these structures is important for diagnosis.

Conclusion: The changes taking place in relation to the central nervous system components have consequences on the patient's life. The implication is that Alzheimer's disease should be studied from different perspectives, including the studying of images to support clinical assessments. Imaging can aid the accuracy of diagnosis through the identification of specific areas and causes connection with particular types of dementia.

Key words: Alzheimer's disease, etiopathogeny, CT investigation, diagnosis, imaging

RÉSUMÉ

Considérations médicales sur la maladie d'Alzheimer

Contexte: La maladie d'Alzheimer est une pathologie fréquente du monde moderne, particulièrement avec le vieillissement des populations. Cela est dû à deux composantes héréditaires et à la suite de nombreuses dégénérescences des structures neuronales et composants du système nerveux central. Par conséquent, la recherche sous différents points de vue est nécessaire pour discerner les mécanismes complexes qui donnent naissance à cette maladie neuro-dégénérative. L'utilisation de l'imagerie est une méthode possible, et le présent document illustre l'utilité de cette approche. **Matériel et méthodes:** Le matériel présenté dans le présent document aborde les questions de l'étiologie de la maladie d'Alzheimer, de ses effets sur les cellules nerveuses et des changements dans le système nerveux central. Pour illustrer cela, les informations relatives aux patients, sous la forme d'images CT, sont détaillées. **Résultats:** Par l'analyse des tests d'imagerie présentés dans ce document, il est noté que les changements se produisent sur les structures du système nerveux central suivant: cerveau, cervelet, cortex cérébral aigu, la substance blanche périventriculaire. En dehors des changements spécifiques, les examens CT montrent aussi que d'autres structures, comme les sinus, cellules mastoïdiennes ou orbites, ne subissent aucun changement. La distinction entre ces structures est importante pour le diagnostic.

Conclusion: Les changements qui ont lieu sur les composants du système nerveux central, ont des conséquences sur la vie du patient. De ce fait, la maladie d'Alzheimer doit être étudiée à partir de différents points de vue, y compris l'étude des images à l'appui des évaluations cliniques. L'imagerie peut supporter la précision du diagnostic grâce à l'identification de domaines spécifiques et les causes liées à certains types de démence.

Mots clés: maladie d'Alzheimer, étiopathologie, Recherche CT, diagnostic, Imagerie

Correspondence address: Antonella Cheșcă, MD, PhD
Basic, Preventive and Clinical Sciences Department
N. Bălcescu Str., no. 56, Brașov, Romania

e-mail: anto.chesca@gmail.com

INTRODUCTION

The causes of Alzheimer's disease are not entirely clear. The disease is characterized by the destruction of nerve cells in specific regions of the brain and the hippocampus, a component located deep in the medial temporal lobe of the brain, involved in controlling memory elapsed duration. With the cessation of the function of neurons in the hippocampus, short-term memory is impaired and the affected person shows signs of an inability to conduct daily activities. [4]

Subsequently Alzheimer's disease affects the cerebral cortex. These are areas responsible for speech and reasoning. Such speech disorders occur with an impaired ability to reason correctly. These disorders grow in severity as the disease progresses. [5] With the deterioration of cognition, several areas of the brain that are affected by atrophy. Here they shrink and lose function and the patient becomes helpless and is immobilized in the bed.

By microscopic morphological examination of the brain of a person with Alzheimer's disease, it is observed that the affected regions undergo changes. The pathological alterations are due to two structures: neurofibrillary tangles and amyloid plaques. [13, 16] Neurofibrillary tangles are insoluble twisted fibers found inside the brain's cells. The occurrence of neurocerebral nodes is characterized by morphological appearance of masses of protein fibers that are located in nerve cells. Normally, this protein is involved with binding and the stabilization of specific portions of neurons. However, in Alzheimer's disease it is chemically and structurally altered, becoming tangled and entwined with morphological and loses function. [1, 8] Amyloid is a general term for protein fragments that the body produces. Amyloid plaques are made of insoluble deposits of beta-amyloid, which is a protein fragment of larger proteins known as amyloid precursor protein - PPA. It is combined with parts of neurons and non-nerve cells. [2, 14] The amyloid plaques are located in a space between nerve cells in the brain. In a normal brain, such fragments are removed; however, with Alzheimer's disease the fragments combine to create hard, insoluble plaques.

Studies to elucidate the mechanism by which these structures operate in Alzheimer's disease have not clarify the specific processes. Many researchers are of the opinion that these mechanisms interfere with normal communication between nerve cells in the brain, leading to nerve cell death. [3, 10] Furthermore, such studies have not elucidated the factors that trigger the formation of these structures and how Alzheimer's disease goes on to develop. Most probably, the disease is the result of many interrelated factors, including genetic factors, environmental factors, joined by as yet unidentified factors.

According to research, there are two types of Alzheimer's disease. Familial Alzheimer's disease is an autosomal dominant inherited disease; whereas Alzheimer's disease non-familial or sporadic, shows no hereditary pattern. Moreover, according to classification by the age at which Alzheimer's disease is characterized by early onset, defined as diagnosis

up until age 65 and 5-10% of cases are diagnosed in age groups between 30-65 years. In the majority of cases, Alzheimer's disease is diagnosed in persons older than 65 years.

Across different demographic groups, early onset Alzheimer's disease is developing most rapidly. In studies it is estimated that most cases of familial Alzheimer's disease were manifest as early onset. Of such cases, 50% are due to three defective genes located on three different chromosomes. With these, the first is the gene for amyloid precursor protein (APP), found on chromosome 21, and which causes the production of an abnormal PAP. The second gene presenilin 1 gene is an altered protein and it is found on chromosome 14, causing an abnormal protein synthesis. The third gene, one for presenilin 2, is located on chromosome 1; it is responsible for the formation of abnormal presenilin 2. [2, 11] Although numerous studies have been performed, there is no recorded evidence to show that these defective genes - involved in causing early onset cases - have any role in the development of Alzheimer's disease in older people.

In the 1990s researchers discovered APOE gene (apolipoprotein E) located on chromosome 19. This is now regarded as perhaps the most important genetic link with (cup-like) Alzheimer's disease appearance. The gene APOE (apolipoprotein E) is involved in the production of a protein with a role in lipid transport in nerve cells. The APOE gene shows at least three forms (alleles), called APOE ϵ 2, APOE ϵ 3, and APOE ϵ 4. According to studies, each person inherits a gene APOE from both parents, resulting in children having either two different genes or two identical copies. In a rare form, APOE ϵ 2 appears to protect some people from Alzheimer's disease or at least slows down the progression of the disease. APOE ϵ 3 is the most common form of the gene and is believed to have a neutral role in disease development. APOE ϵ 4 appears to increase the risk of developing Alzheimer's disease at earlier ages. [9] Here, studies have shown that people who have at least one copy of the APOE ϵ 4 show a 3 times greater risk of developing the disease; while those with two copies have four times higher risk of developing the disease.

Oxidative stress mechanisms, nitric oxide mechanism implied in microglial activation to neuronal cell injury, and proper calcium homeostasis, are also important points for Alzheimer's disease diagnosis. [6, 7, 15]

Although there have been numerous studies to date, such research has not elucidated the causes of developing Alzheimer's disease. What has been found is that disease etiopathogenesis relates to several risk factors that increase a person's susceptibility to develop the disease. Of the risk factors implicated in causing disease, the most important is age older people are more susceptible than young people. Also there is evidence that stroke is related to the onset of Alzheimer's disease, especially those of low intensity and which are not clinically apparent, but where nerve cells are affected. [12] Another risk factor is increased serum cholesterol, which may play a role in causing Alzheimer's disease. With the latter, once diagnosed, and appropriate therapy instituted palliative measures and related hygienic-

dietary measures administered over the life of the patient, can improve the patient's quality of life.

In this case report, we provide results of imaging tests, from a patient diagnosed with Alzheimer's disease. We discuss these in relation to the discussed research findings.

CASE REPORT

Imaging methods of investigation are regarded as means of diagnosing neurodegenerative diseases. In this context, we present data in relation to computed tomography (CT) scanning performed in relation to a case that clinical examination suggested showed signs of neurodegenerative diseases. Native CT was performed using helical acquisition centered cranial with multiplanar reconstructions. The investigation was useful for the diagnosis of neurodegenerative disease in a female patient aged 82 years, resident in an urban area. The result of the investigation reported no bleeding in the brain parenchyma lesions with small presence of lacunar infarctions, capsulolenticular bilaterally.

The imaging was observed, median topography structures preserved trenches and cerebellar cortical brain sharp, brain ventricles increased in size and symmetrical layout were assessed. CT scanning showed minimal hypodensity native of bilateral periventricular white matter. The imaging examination revealed the Turkish saddle and pituitary gland were of a normal aspect.

Furthermore:

- *There were no reported abnormalities in bilateral pontine cerebellar angle.*
- *Paranasal sinuses and mastoid cells were normal pneumatized in this case investigated.*
- *Orbits show apparently normal, examination without showing changes at the normal bone structure.*

The following images, below, capture aspects from computed tomograph data acquisitions, as X-ray images of cross-sections of the brain. They relate to a patient with Alzheimer's disease and show the axial, coronal and sagittal section. (Figs. 1, 2, 3) Changes in the neuronal structures, according to this neurodegenerative disease, are apparent.

DISCUSSION

As defined by the pathology alterations of psychosomatic disease, the Alzheimer's disease patient requires close monitoring once the diagnosis is established. As disease is a high frequency pathology among elderly patients, standardized geriatric assessment is needed for diagnosis. This involves a discussion for about two hours between specialized healthcare professionals to monitor the signs and symptoms. To accurately establish the diagnosis of Alzheimer's disease this involves an interdisciplinary collaboration between members of the medical team, including a neurologist, a psychiatrist, a geriatrician, medical laboratory practitioners; and the use of medical imaging. The information discussed above needs to go hand-in-hand with data related comor-

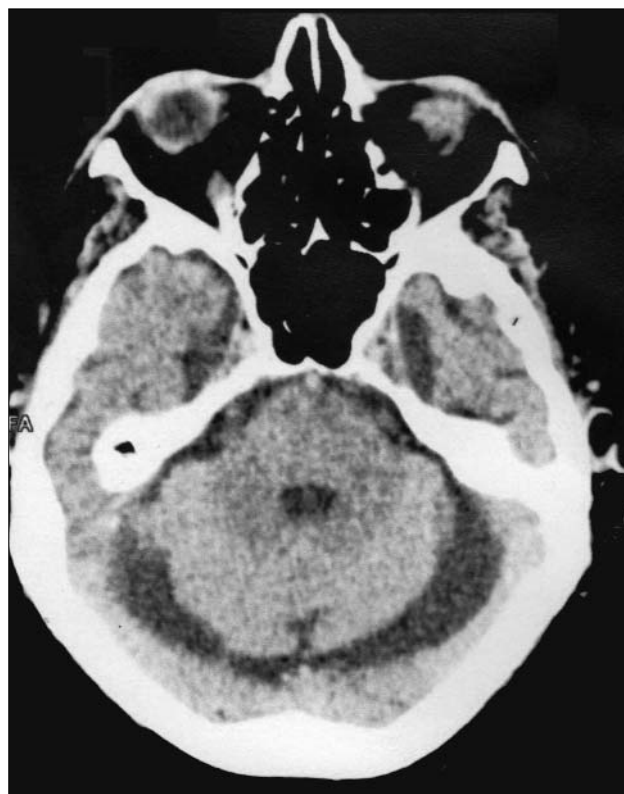


Figure 1 - CT image – axial

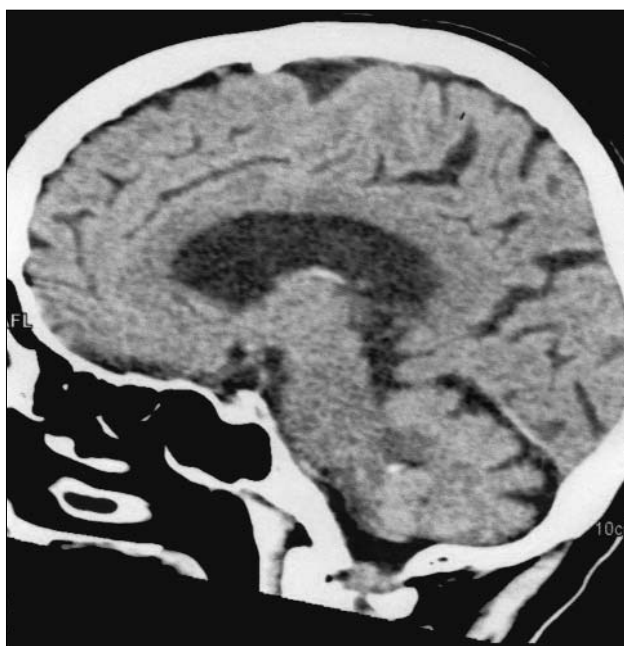


Figure 2 - CT image – coronal

bidities for the patient diagnosed with Alzheimer's disease. Once a diagnosis is confirmed geriatric family counseling is important. The stage of disease and the family attitude to be adopted towards the patient and their needs are very important to ensure the quality of life of the patient maintained at the optimal level.



Figure 3 - CT image – sagittal

CONCLUSIONS

The conclusion of the analysis carried out computed tomography investigation indicates the changes that occur in the form of cerebral atrophy with a patient clinically diagnosed with Alzheimer's disease, generally in relation to the medial temporal lobe. Thus imaging investigation is useful to support a clinical diagnosis of neurodegenerative disease. Moreover, imaging can help to track the progression of the disease in affected patients.

REFERENCES

1. Chao CC, Hu S, Molitor TW, Shaskan EG, Peterson PK. Activated microglia mediate neuronal cell injury via a nitric oxide mechanism. *J Immunol.* 1992 Oct 15;149(8):2736-41.
2. Chao CC, Molitor TW, Hu S. Neuroprotective role of IL-4 against activated microglia. *J Immunol.* 1993;151(3):1473-81.
3. Pike CJ, Burdick D, Walencewicz AJ, Glabe CG, Cotman CW. Neurodegeneration induced by beta-amyloid peptides in vitro: the role of peptide assembly state. *J Neurosci.* 1993 ; 13(4):1676-87.
4. Yankner BA, Duffy LK, Kirschner DA. Neurotrophic and neurotoxic effects of amyloid beta protein: reversal by tachykinin neuropeptides. *Science.* 1990 Oct 12;250(4978):279-82.
5. Araujo DM, Cotman CW. Beta-amyloid stimulates glial cells in vitro to produce growth factors that accumulate in senile plaques in Alzheimer's disease. *Brain Res.* 1992 Jan 8;569(1): 141-5.
6. Coyle JT, Puttfarcken P. Oxidative stress, glutamate, and neurodegenerative disorders. *Science.* 1993 Oct 29;262(5134): 689-95.
7. Behl C, Davis JB, Lesley R, Schubert D. Hydrogen peroxide mediates amyloid beta protein toxicity. *Cell.* 1994 ; 77(6):817-27.
8. Selkoe DJ, Bell DS, Podlisny MB, Price DL, Cork LC. Conservation of brain amyloid proteins in aged mammals and humans with Alzheimer's disease. *Science.* 1987 Feb 20; 235(4791):873-7.
9. Boje KM, Arora PK. Microglial-produced nitric oxide and reactive nitrogen oxides mediate neuronal cell death. *Brain Res.* 1992 Aug 7;587(2):250-6.
10. Olanow CW. A radical hypothesis for neurodegeneration. *Trends Neurosci.* 1993 Nov;16(11):439-44.
11. Otvos L Jr, Szendrei GI, Lee VM, Mantsch HH. Human and rodent Alzheimer beta-amyloid peptides acquire distinct conformations in membrane-mimicking solvents. *Eur J Biochem.* 1993 Jan 15;211(1-2):249-57.
12. Mullan M, Crawford F. Genetic and molecular advances in Alzheimer's disease. *Trends Neurosci.* 1993 Oct;16(10):398-403.
13. Cheng B, Christakos S, Mattson MP. Tumor necrosis factors protect neurons against metabolic-excitotoxic insults and promote maintenance of calcium homeostasis. *Neuron.* 1994;12(1):139-53.
14. Corradin SB, Mauël J, Donini SD, Quattrocchi E, Ricciardi-Castagnoli P. Inducible nitric oxide synthase activity of cloned murine microglial cells. *Glia.* 1993 Mar;7(3):255-62.
15. Perry VH, Andersson PB, Gordon S. Macrophages and inflammation in the central nervous system. *Trends Neurosci.* 1993 Jul;16(7):268-73.
16. Villalba M, Martínez-Serrano A, Gómez-Puertas P, Blanco P, Börner C, Villa A, Casado M, Giménez C, Pereira R, Bogonez E, et al. The role of pyruvate in neuronal calcium homeostasis. Effects on intracellular calcium pools. *J Biol Chem.* 1994 Jan 28;269(4):2468-76.