A case study of Alzheimer’s disease with work-related exposure to aluminium

Vityala Yethindra*1, Gulzat Mataeva2, Baian Beknazarova2, Furquan Nazami1, Yogesh parihar1, Mohammad Shaour Khalid1, Alenur Narsimharaj1

1International Higher School of Medicine, International University of Kyrgyzstan, 1F, Intergelpo street, Bishkek, Kyrgyzstan, 720054
2Department of Special Clinical disciplines, International Higher School of Medicine, International University of Kyrgyzstan, 1F, Intergelpo street, Bishkek, Kyrgyzstan, 720054

ABSTRACT
Aluminium (Al) is a neurotoxin, and its work-related exposure can lead to Alzheimer’s disease (AD). In this case study, we describe the increased levels of Al in brain samples of a patient diagnosed with AD, who reportedly had work-related exposure to Al. In 2019, an Asian male died at the age of 64 with AD. His brain samples showed increased Al levels. The mean Al presence in tissues (n = 21) was 4.72, with a SD of 3.4 μg/g DW and a range from 0.00 – 18.35 μg/g DW. During his work in a large-scale aluminium factory, his work involved exposure to Al for five years on weekly four days basis. In our case study, we investigated the Al content of brain tissue in AD, and Al levels were seen raised and related to neurodegeneration. Work-related exposure to Al in a patient initially showed mild symptoms then lead to memory issues, and after years he was diagnosed with AD. Many clinical trials and researches are needed to find more possible effects of Al content in the human brain.

INTRODUCTION
Aluminium (Al) is a neurotoxin, and its work-related exposure can lead to Alzheimer’s disease (AD). Early-onset Alzheimer’s disease (EOAD) is a very rare neurodegenerative disorder. Individuals are feeling burgeoning exposure to Al in daily life (Exley, 2013). Al accumulation in the brain is linked with several neurodegenerative diseases (Exley and House, 2011). Neurodevelopmental effects were related to occupational exposure to Al; (Meyerbaron et al., 2007; Riihimäki and Aitio, 2012) fewer data existed about brain Al content in occupationally exposed people (McLaughlin et al., 1962). In this case study, we describe the increased levels of Al in brain samples of a patient diagnosed with AD, who reportedly had work-related exposure to Al.

Case study
A 55-year-old male patient was diagnosed with AD in 2010. The patient had no past medical history. Six years ago, he got recruited to work in a large-scale aluminium factory. This work leads him to inhale aluminium sulfate [Al2(so4)3] dust for five years on a weekly four days basis. During work time, he used provided work clothes, masks, and gloves. But he used an ordinary mask to defend against the inhalation of the Al dust. After two months of recruitment at work, he had complaints such as headache, fatigue, and mouth ulcers. From 2008 he started complaining issues associated with mem-
Table 1: Al content of 25 tissue samples collected from frontal lobe section of a person with AD

| Brain samples | Al µg/g DW |
|---------------|------------|
| 1             | 4.64       |
| 2             | 0.92       |
| 3             | 3.46       |
| 4             | 2.59       |
| 5             | <MB        |
| 6*            | 63.98      |
| 7             | 3.84       |
| 8             | 2.36       |
| 9             | 3.72       |
| 10            | 1.48       |
| 11            | 1.96       |
| 12            | 12.86      |
| 13            | 18.35      |
| 14            | <MB        |
| 15            | 12.21      |
| 16            | 4.02       |
| 17            | 2.61       |
| 18            | 8.55       |
| 19            | 0.86       |
| 20            | 2.73       |
| 21            | 2.61       |
| 22            | 0.69       |
| 23            | 3.76       |
| 24            | 5.06       |
| 25*           | 21.25      |
| Mean (SD)     | 4.72 (3.4) |

Al, aluminium; DW, Dry weight; MB, method blank; SD, Standard deviation; *Not considered for mean

ory and showed depression. In 2019, he died at the age of 64 and samples of his brain tissues were sent for diagnosis to neurology clinic and frozen frontal lobe (FL) section was examined for tissue Al confirmation. Diagnosis showed bountiful of β amyloid plaques, and cerebral cortex areas have many neurofibrillary tangles (NFTs). The FL tissue was defrosted and split into 25 equivalent sized samples each weighed 250 mg. To get constant DW, for 72 hours, tissues were placed in an incubator at 37°C. 1:1 mixture of 15.8M nitric acid and 30% w/v hydrogen used for digestion of dry tissues in a microwave oven. Two tissue samples (5, 14) with the presence of Al were less than method blank and noted as zero. In two tissue samples (6, 25), DWs were less than 10 mg, Al presence in these two samples are neglected. For statistical purposes, tissue samples were noted zero and neglected. The mean Al presence in tissues (n = 21) was 4.72, with a SD of 3.4 µg/g DW and a range from 0.00 – 18.35 µg/g DW (Table 1).

DISCUSSION

The total range of Al content was noted, verifying the expected focal aggregation of Al in brain tissue, and mean value for 21 samples, 4.72 µg/g DW, four times greater, i.e., 0.83 µg/g DW in the past noted for samples of FL from different peoples (House et al., 2012). Exclusion of two high values 30% of the Al content measured were more than 3.50 µg/g DW, and they are pathological (House et al., 2012).

Analyzing 25 tissue samples from the FL has shown unequivocal proof of high amounts of Al presence in a patient when he is subjected to work-related exposure to Al for five years. The diagnosis of EOAD resulting autopsy of AD at age 64 is indicative of beligerent disease cause and the expected action of Al in the early and progressing condition. The role of Al content in AD is not adequately described, but our case study shows bright pieces of evidence, such as patient’s work-related exposure to Al showed EOAD
and more rapid progression.

A case report of an individual occupationally exposed to Al directly linked to AD as part of progression (Exley and Vickers, 2014). Excessive amounts of Al in brain tissue are neurotoxic and cause intoxication.

Elevated levels of Al present in the brain are responsible for EOAD and its rapid progression. Even in some studies, because of high Al exposure, lead to elevated levels of Al in the brains of AD patients (Exley, 2006; Mirza et al., 2017).

CONCLUSIONS

In our case study, we investigated the Al content of brain tissue in AD, and Al levels were seen raised and related to neurodegeneration. Work-related exposure to Al in a patient initially showed mild symptoms then lead to memory issues, and after years he was diagnosed with AD. Many clinical trials and researches are needed to find more possible effects of Al content in the human brain.

ACKNOWLEDGEMENT

As Vityala Yethindra, I am very thankful to my parents Vityala Anitha and Vityala Thirupathi, for their valuable support in continuing research. I wish to thank Dr Ishenbek Satylganov, Dr Mamatov Sagynali Murzaevich, Dr Panchadcharam Harinath, Dr Tugolbait Tagaev, Dr Cholpon Dzhumakova, Dr Elmira Mainazarova, and Dr Asel Namazbekova for their useful criticisms and discussion of this manuscript.

Ethical Considerations

There is no ethical principle to be considered during this research.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare no conflict of interest

REFERENCES

Exley, C. 2006. Severe cerebral congophilic angiopathy coincident with increased brain aluminium in a resident of Camelford, Cornwall, UK. Journal of Neurology, Neurosurgery & Psychiatry, 77(7):877–879.

Exley, C. 2013. Human exposure to aluminium. Environ. Sci.: Processes Impacts, 15(10):1807–1816.

Exley, C., House, E. R. 2011. Aluminium in the human brain. Monatshefte für Chemie - Chemical Monthly, 142(4):357–363.

Exley, C., Vickers, T. 2014. Elevated brain aluminium and early onset Alzheimer’s disease in an individual occupationally exposed to aluminium: a case report. Journal of Medical Case Reports, 8(1):41–41.

House, E., Esiri, M., Forster, G., Ince, P. G., Exley, C. 2012. Aluminium, iron and copper in human brain tissues donated to the medical research council’s cognitive function and ageing study. Metallomics, 4(1):56–65.

McLaughlin, A. I. G., Kazantzis, G., King, E., Teare, D., Porter, R. J., Owen, R. 1962. Pulmonary Fibrosis and Encephalopathy Associated with the Inhalation of Aluminium Dust. Occupational and Environmental Medicine, 19(4):253–263.

Meyerbaron, M., Schaper, M., Knapp, G., Vanthrier, C. 2007. Occupational aluminium exposure: Evidence in support of its neurobehavioral impact. NeuroToxicology, 28(6):1068–1078.

Mirza, A., King, A., Troakes, C., Exley, C. 2017. Aluminium in brain tissue in familial Alzheimer’s disease. Journal of Trace Elements in Medicine and Biology, 40:30–36.

Riihimäki, V., Aitio, A. 2012. Occupational exposure to aluminum and its biomonitoring in perspective. Critical Reviews in Toxicology, 42(10):827–853.