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Eosinophilic astrocytic inclusions of the white matter in a patient with epilepsy: A case report

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ABSTRACT

Protein aggregations are commonly seen in many conditions associated with epilepsy. They are usually present in cortical-based inclusions; they have different types, which present with different characteristics. In this rare case, we have a patient with astrocytic inclusions predominantly in the white matter. We present his case and the characteristics of the inclusion bodies.

Keywords: Epilepsy, seizure, astrocytic inclusions, filamin.

1. INTRODUCTION

Epilepsy is a neurological disorder characterized by multiple and recurrent unprovoked seizures and associated with many pathological changes in the affected areas (Fisher et al., 2014). Those changes are closely related to the pathology of the epilepsy or to the effects of epilepsy on the brain tissue. Glial and neuronal inclusions are known in neuropathological conditions such as neurodegenerative diseases, viral infections, low-grade tumors, and seizure-related disorders. Rarely, astrocytic inclusions are associated with epilepsy disorders, and they are present almost always in cortical-based inclusions (Takao et al., 2004).

2. CASE REPORT

Our patient is a 39-year-old man with a longstanding history of epilepsy. His magnetic resonance imaging (MRI) showed a focal right frontal cortical lesion, which appeared high in T2 with no restricted diffusion and was not enhanced in post-contrast images. It measured 1.6 x 1.4 x 2.0 cm (Figures A-C). The patient underwent a diagnostic biopsy. The histological examination of the biopsy showed small pieces of unoriented gray matter and white matter. The cerebral cortex showed focal neuronal clustering. Dysmorphic and balloon neurons were not seen. Neuronal inclusions were not present. Neither neuronophagia nor well-formed microglial nodules were identified. There was no evidence of malignancy. The white matter was rarefied and hypercellular. Numerous bright, round to oval, eosinophilic astrocytic inclusions were seen throughout the white matter (Figures D-E), and they

were located predominantly in the processes of the astrocytes. They were GFAP-positive (Figure F) and were negative for neuro-lament, Alpha B crystallin, PAS, Congo-red, Alcian-blue, and Ziehl-Neelsen stains (Figure G). GFAP stain also highlighted gliosis in both grey and white matter. NeuN was positive only in neurons, and neuro-lament was positive in axons. IDH-1(R132H) was negative, and CD34 was limited to blood vessels.

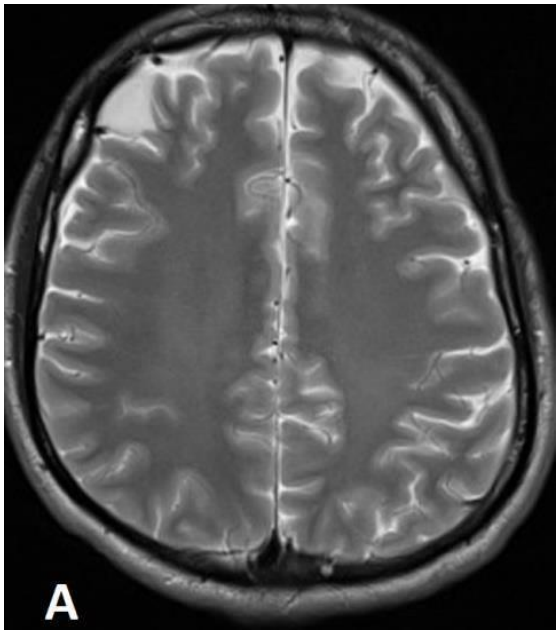

Figure A T2-weighted axial MRI

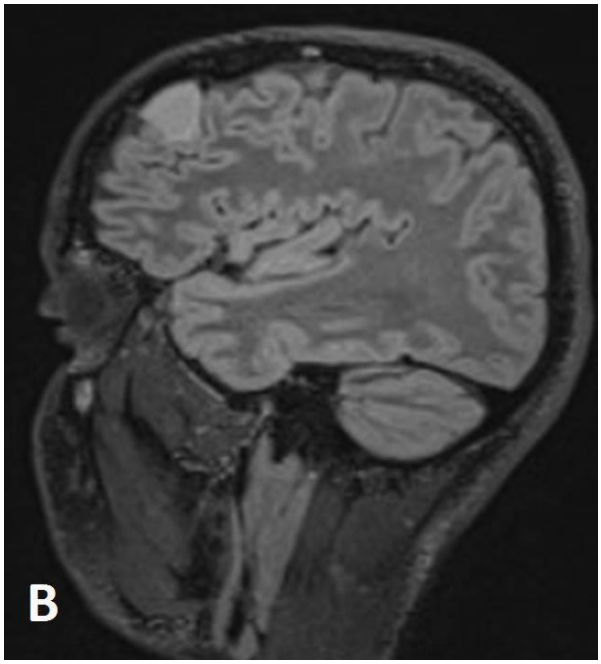

Figure B T2-weighted flair sagittal MRI

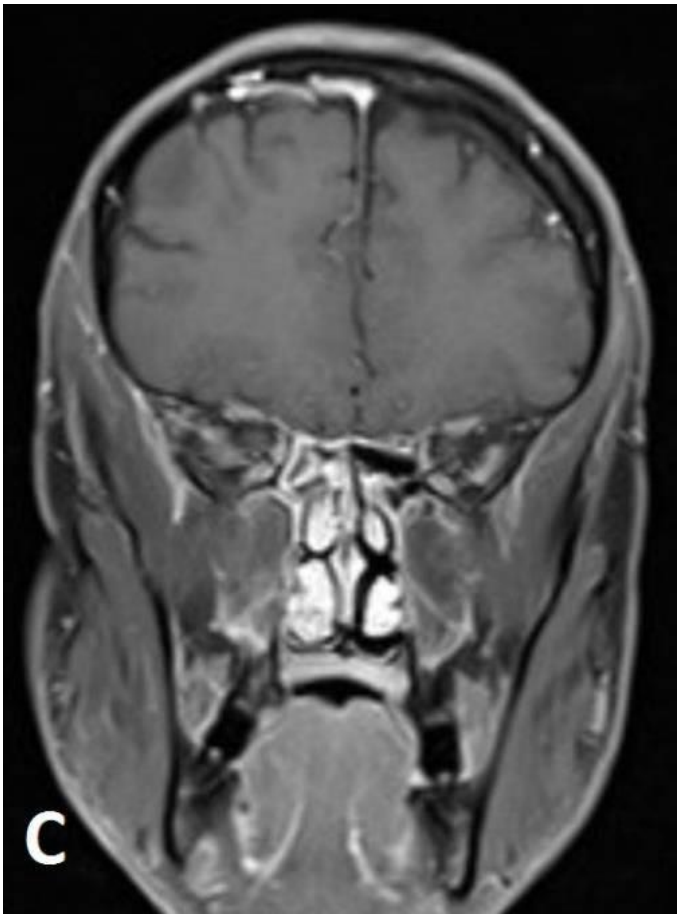

Figure C T1-weighted coronal post contrast MRI.

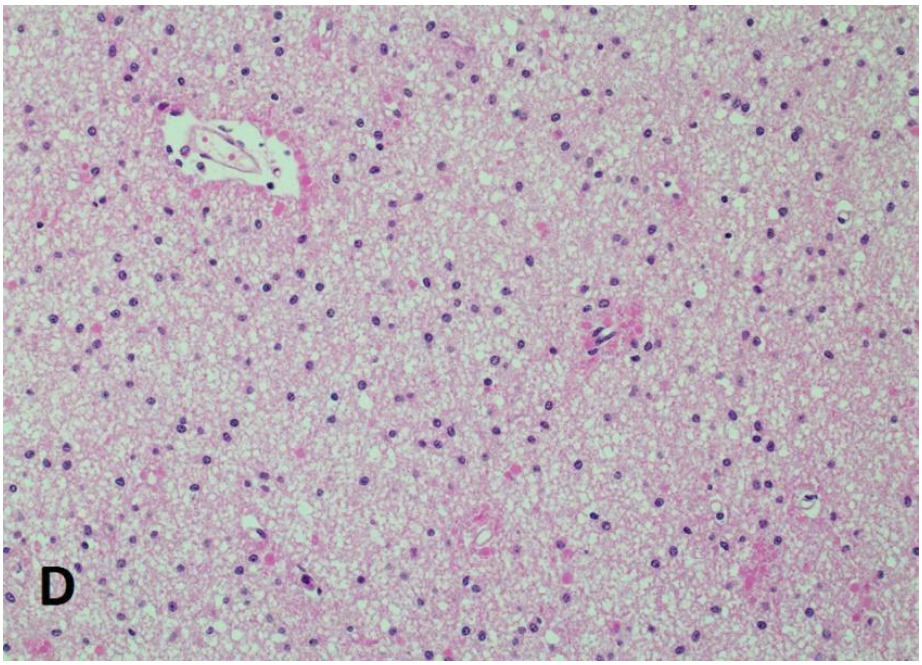

Figure D H & E-stained slide showing numerous bright, round to oval, eosinophilic astrocytic inclusions X20.

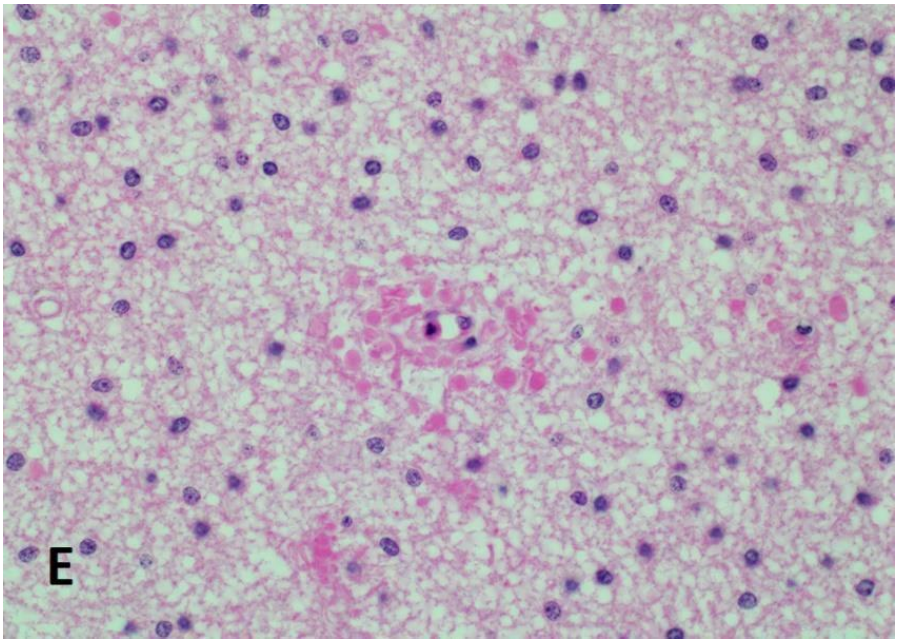

Figure E H & E-stained slide showing numerous bright, round to oval, eosinophilic astrocytic inclusions X40.

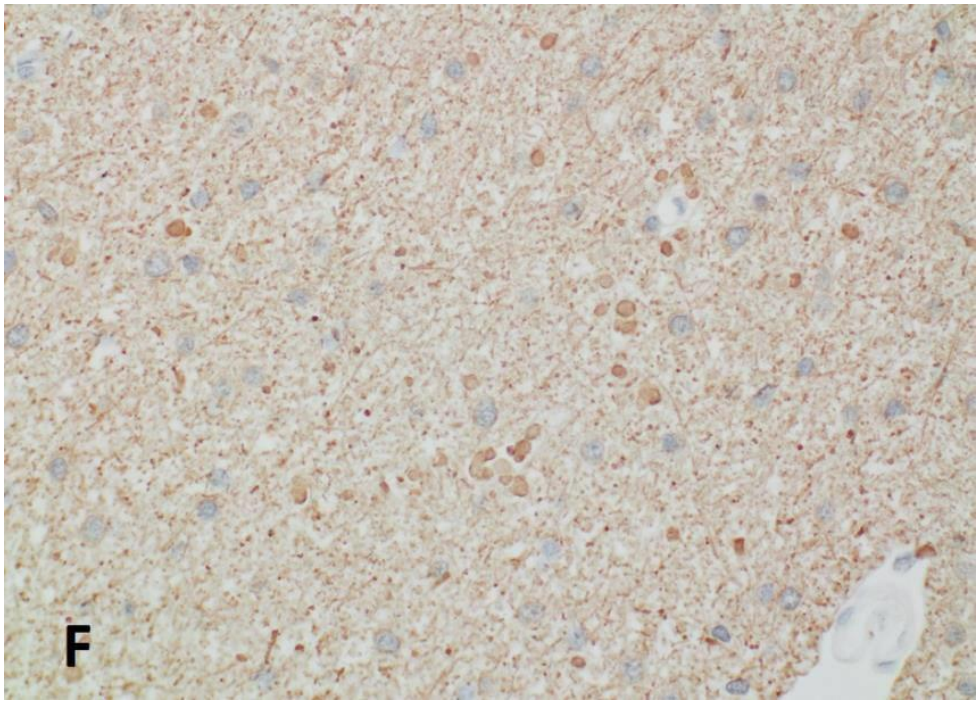

Figure F GFAP staining slide.

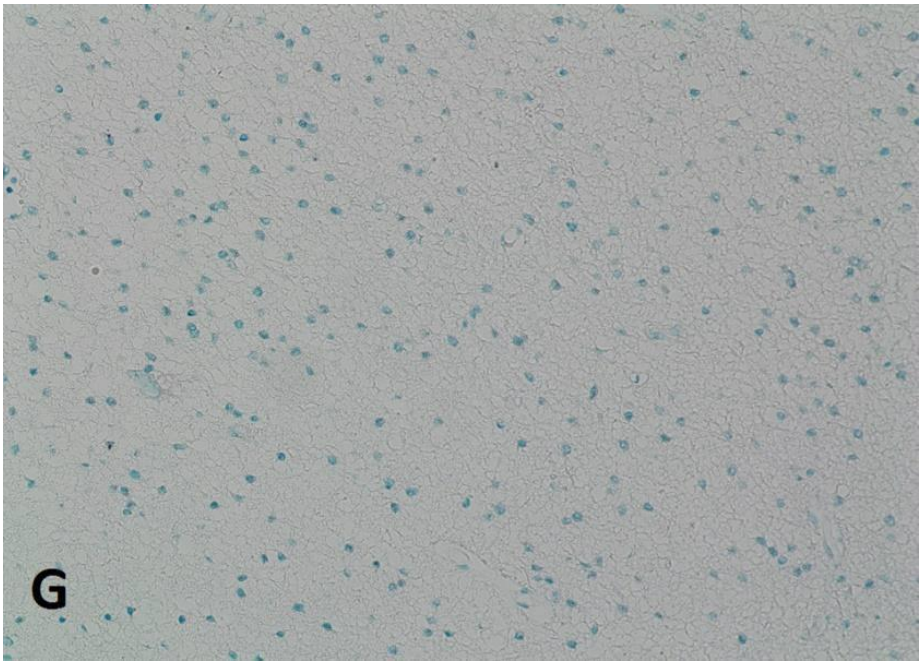

Figure G ZN staining slide.

3. DISCUSSION

Inclusions are commonly seen with different types of neurological diseases. They can be neuronal or glial inclusions, cytoplasmic or nuclear inclusions. They are characteristic features of several neurodegenerative diseases, such as tau inclusions in the form of neuro-fibrillary tangles in Alzheimer's disease (Braak and Braak, 1997) and picks bodies in picks disease (Dickson, 1998), alpha-synuclein inclusions in the form of Lewy bodies in Parkinson's disease (Rocha et al., 2018) and polyglutamine inclusions in Huntington disease (Ha and Fung, 2012). Large storage inclusions are features of many neurometabolic diseases like lysosomal storage disorders (Schultz et al., 2011). Also, inclusions are commonly associated with viral infections, such as Negri bodies with encephalitis and oligodendrocytic viral inclusions in progressive multifocal leukoencephalopathy. Lafora bodies are seen in patients with myoclonic epilepsy in lafora body diseases. They are round neuronal and astrocytic cytoplasmic inclusions similar to corpora amylacea inclusions.

There are different types of astrocytic inclusions that are associated with conditions such as chronic reactive disorders, neoplastic proliferation, and aging, including eosinophilic granular bodies (EGBs), Rosenthal fibers, corpora amylacea, and astrocytic inclusions that are immunopositive for filamin–A. Rosenthal fibers are bright eosinophilic astrocytic inclusions of different shapes and sizes, and they are usually seen with low-grade glial/glioneuronal tumors such as pilocytic astrocytoma, chronic reactive gliosis, Alexander disease, and giant axonal neuropathies. They are immunopositive for GFAP, αB-crystallin, and ubiquitin. Eosinophilic granular bodies are cytoplasmic astrocytic clusters of round eosinophilic granules that are GFAP and αB-crystallin positive, and they are usually seen like Rosenthal fibers in chronic reactive gliosis and low-grade glial/glioneuronal tumors.

Corpora amylacea are spherical astrocytic inclusions, predominantly in astrocyte processes, and they are positive with hematoxylin, PAS, and methyl violet. With aging, the number of Corpora amylacea increases in subpial and subependymal areas and around blood vessels. Also, they increase in number in some neurodegenerative diseases like Alzheimer's disease and in patients with longstanding epilepsy. Astrocytic inclusions that are immunopositive for filamin–A (Feng and Walsh, 2004), which is an actin-binding protein involved in neuronal migration, are seen in patients with seizure disorder with mild-to-moderate developmental delay and were reported by (Hazrati et al., 2008; Hedley-Whyte et al., 2009). Those inclusions are highly refractile, bright Eosinophilic, amorphous, often semilunar in shapes with irregular angulated boundaries, juxtanuclear, spared distal subpial, or perivascular astrocytic processes, and are cortically located. They are slightly positive for Ziehl Neelsen and s100 and are negative for GFAP, neuro-lament, α-B-crystallin, PAS, Alcian-blue, and Congo-red. These inclusions are seen with patients with Aicardi syndrome.

The similarities with the inclusions seen with Aicardi syndrome strongly suggest the pathology of filamin–A protein (Kato et al., 1992; Minamitani et al., 1994; Abe et al., 1990; Minagawa et al., 1992; Horoupian et al., 2003). Accumulation of Tau proteins in

different sizes and shapes, such as tufted astrocytes and Thorn-shaped astrocytes, are seen in some of the neurodegenerative disorders like progressive supranuclear palsy. The inclusions of our case are unique and different from other types of inclusions. They are round to oval in shape, like corpora amylecea, but they are not basophilic and do not have a laminated appearance. Unlike filamin–A inclusions, they are predominantly in the perivascular astrocytic processes of the white matter and are positive for GFAP and negative for Ziehl Neelsen and s100 in comparison to Rosenthal fibers, they are α-B-crystallin negative, and they spared the subpial areas.

4. CONCLUSION

We report a case of astrocytic inclusions predominantly in the white matter in a patient with longstanding epilepsy. These inclusions are not similar to the previously reported inclusions in patients with epilepsy, such as inclusions with filaminopathy. These inclusions could be the cause or the result of the longstanding seizure. Further studies are needed to determine the exact nature of the inclusions to understand the pathology better.

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Author's contribution

Alaa Alkhotani: Conceptualization, Data curation, Formal analysis, Investigation, Supervision, Validation

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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