

## Online supplemental file 1

### Connexin-43 and Aquaporin-4 are markers of ARTAG-related astroglial response

Gabor G. Kovacs<sup>1,2</sup>†, Ahmed Yousef<sup>2</sup>†, Sabine Kaindl<sup>1</sup>, Virginia M. Lee<sup>2</sup>, John Q. Trojanowski<sup>2</sup>

1: Institute of Neurology, Medical University of Vienna, Vienna, Austria; 2: Center for Neurodegenerative Disease Research, Institute on Aging and Department of Pathology and Laboratory Medicine of the Perelman School of Medicine at the University of Pennsylvania; Philadelphia, PA, USA;

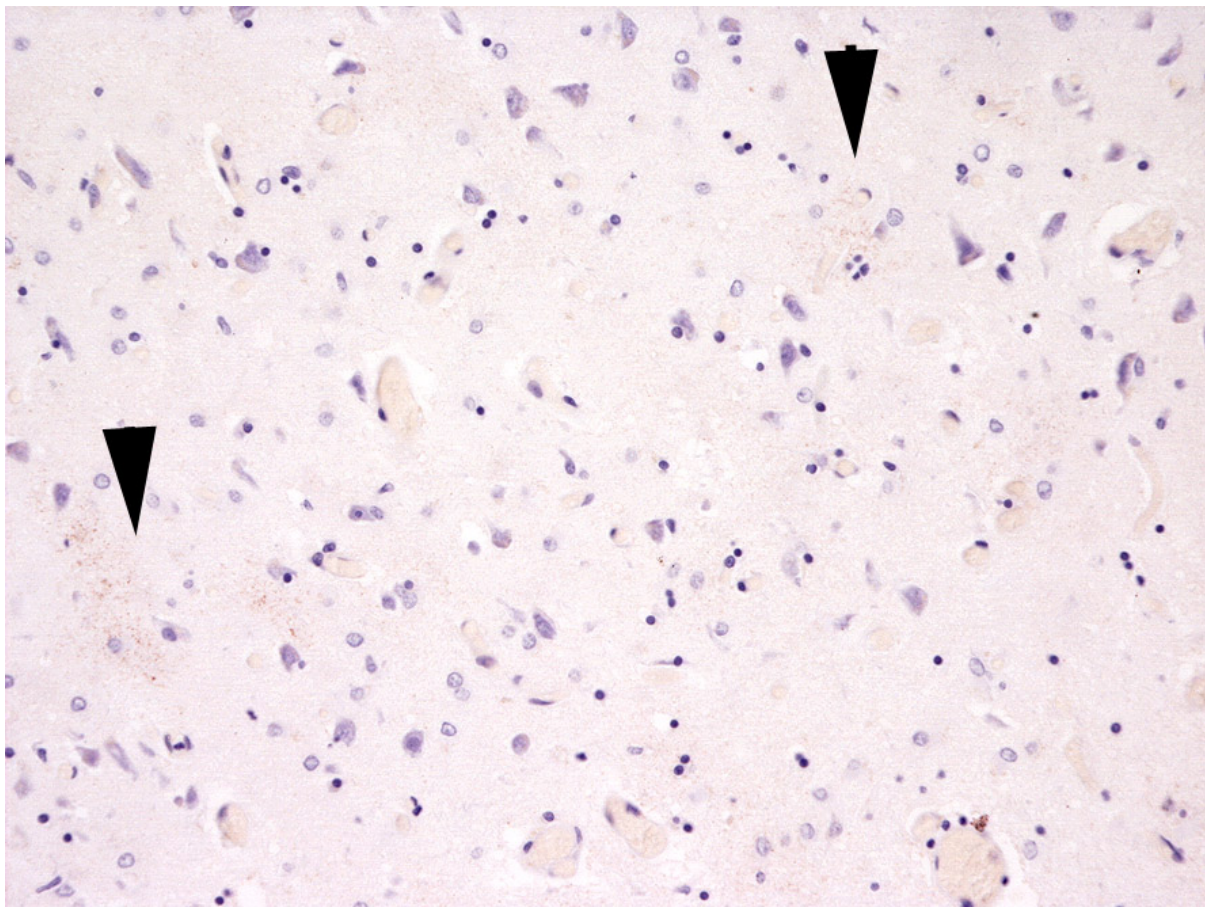
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Immunostaining for Connexin-43 (Cx43) in brain sections showing prominent reactive astrogliosis.

We examined the following cases:

Case Nr	Age (years)	Gender	Neuropathology	Region
1	51	female	Chronic Ischemic/hypoxic panencephalopathy	Hippocampus
2	65	male	Chronic Ischemic/hypoxic panencephalopathy	Hippocampus
3	38	male	Chronic Ischemic/hypoxic panencephalopathy	Hippocampus
4	52	male	Creutzfeldt-Jakob disease	Frontal
5	60	female	Creutzfeldt-Jakob disease	Thalamus
6	60	female	Creutzfeldt-Jakob disease	Frontal

**Case 1:** Cx43 does not show enhanced immunoreactivity in reactive astrocytes but the physiological staining (arrowheads) was recognized in a few astrocytes (magnification: x200).



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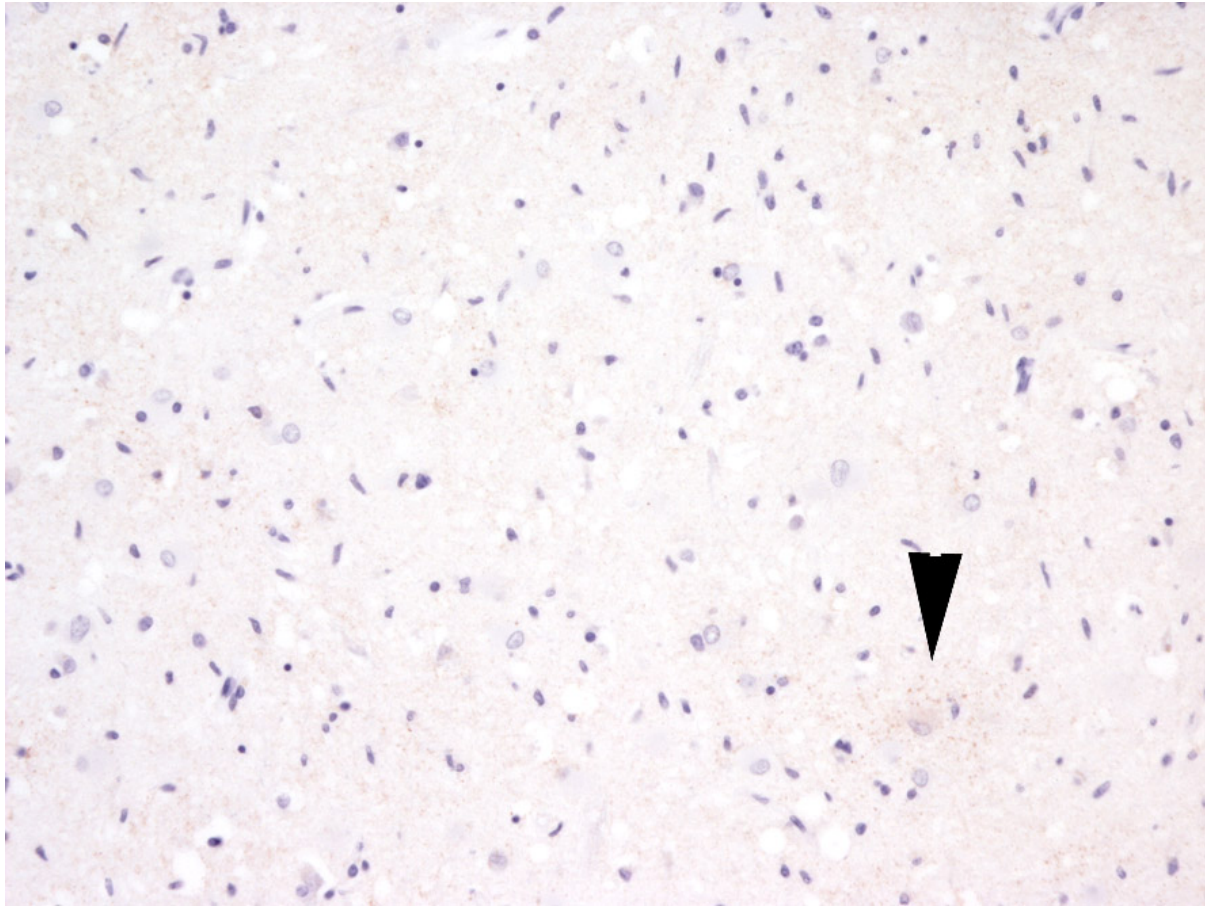
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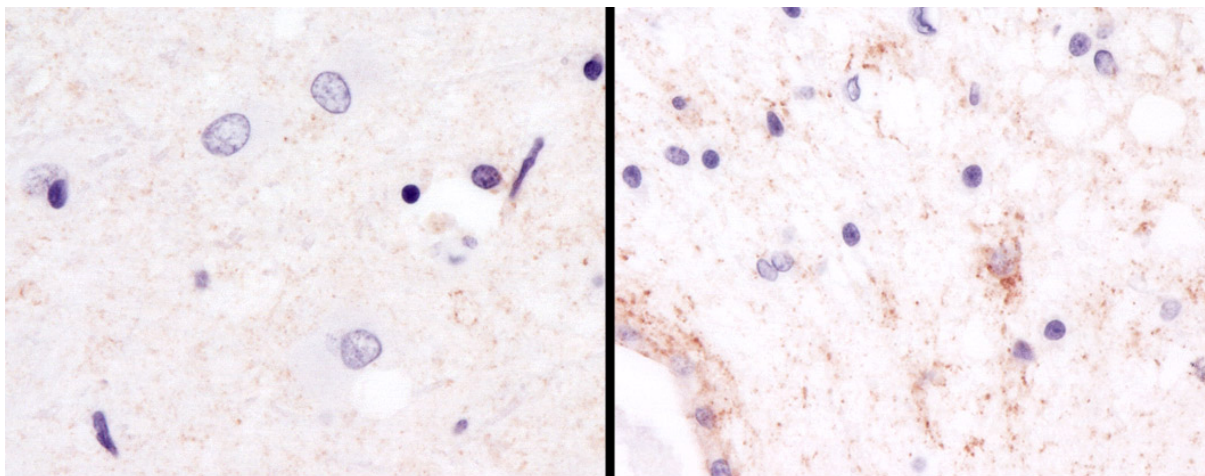
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**Case 2:** Cx43 does not show enhanced immunoreactivity in reactive astrocytes but the physiological staining (arrowhead) was recognized in a few astrocytes (magnification: x200).



In the same case, the enlarged image of a reactive astrocyte (left side of image) shows a lack of prominent Cx43 immunoreactivity, but subependymal astrocytes (right side of image) show physiological strong immunoreactivity.



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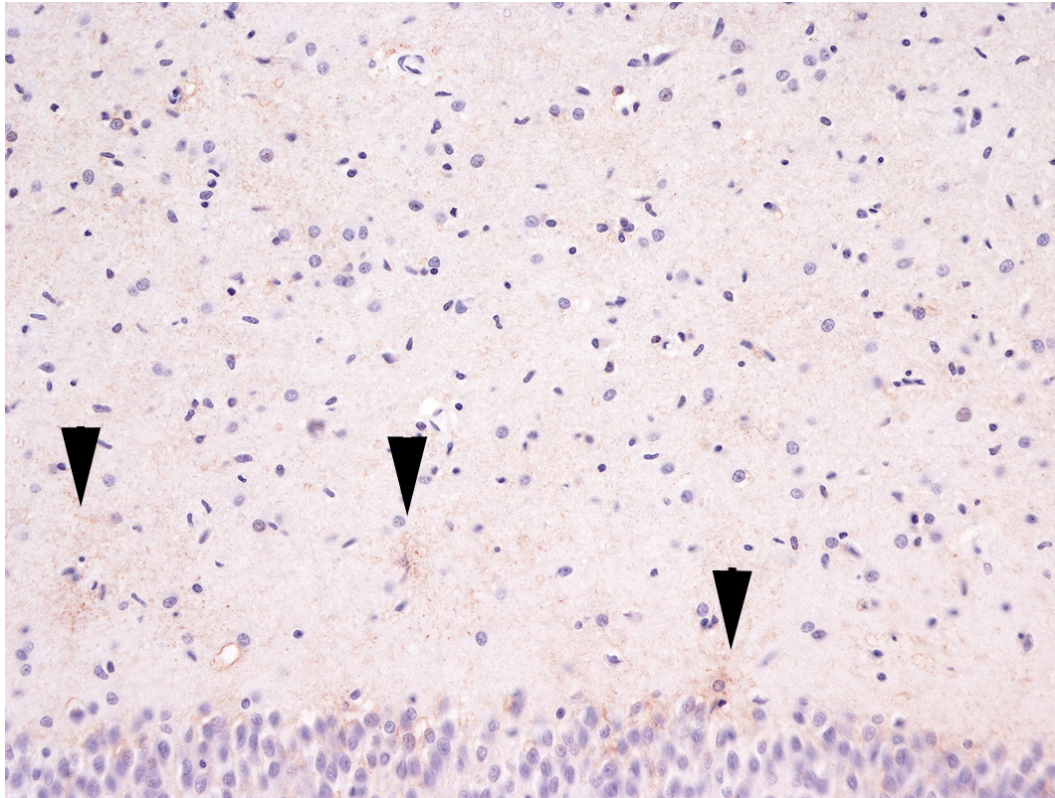
#### **Connexin-43 and Aquaporin-4 are markers of ARTAG-related astroglial response**

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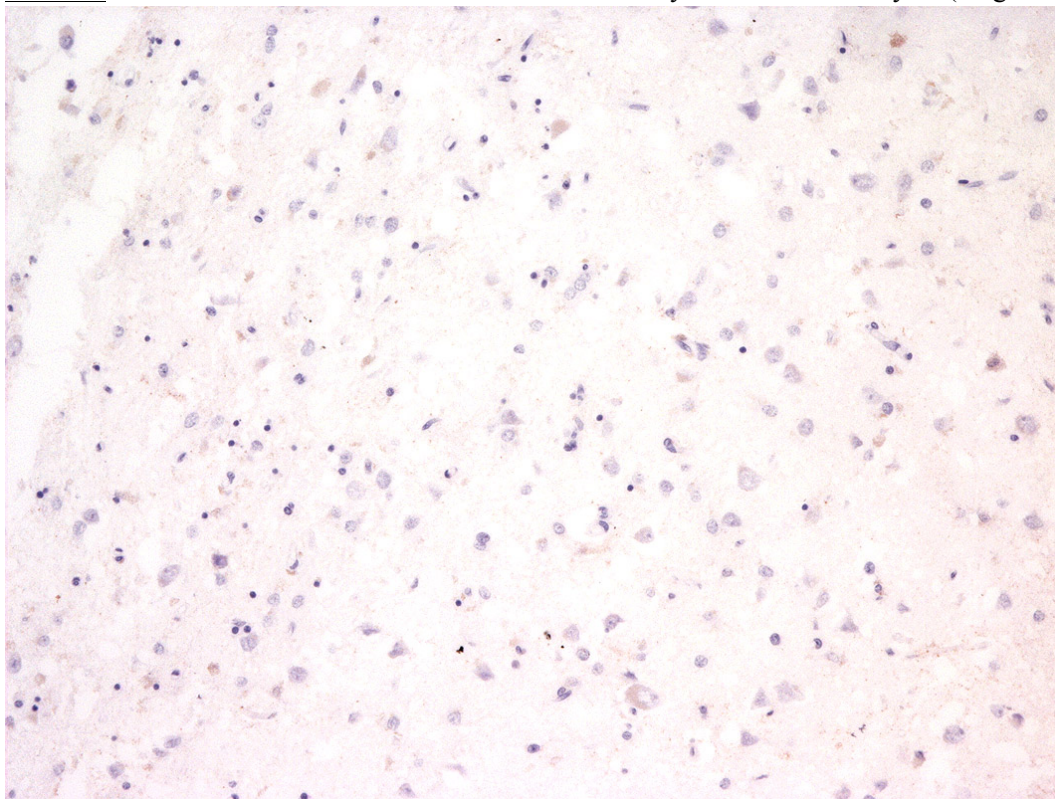
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**Case 3:** Cx43 does not show enhanced immunoreactivity in reactive astrocytes but the physiological staining (arrowheads) was recognized in a few astrocytes (magnification: x200).



**Case 4:** Cx43 does not show enhanced immunoreactivity in reactive astrocytes (magnification: x200).



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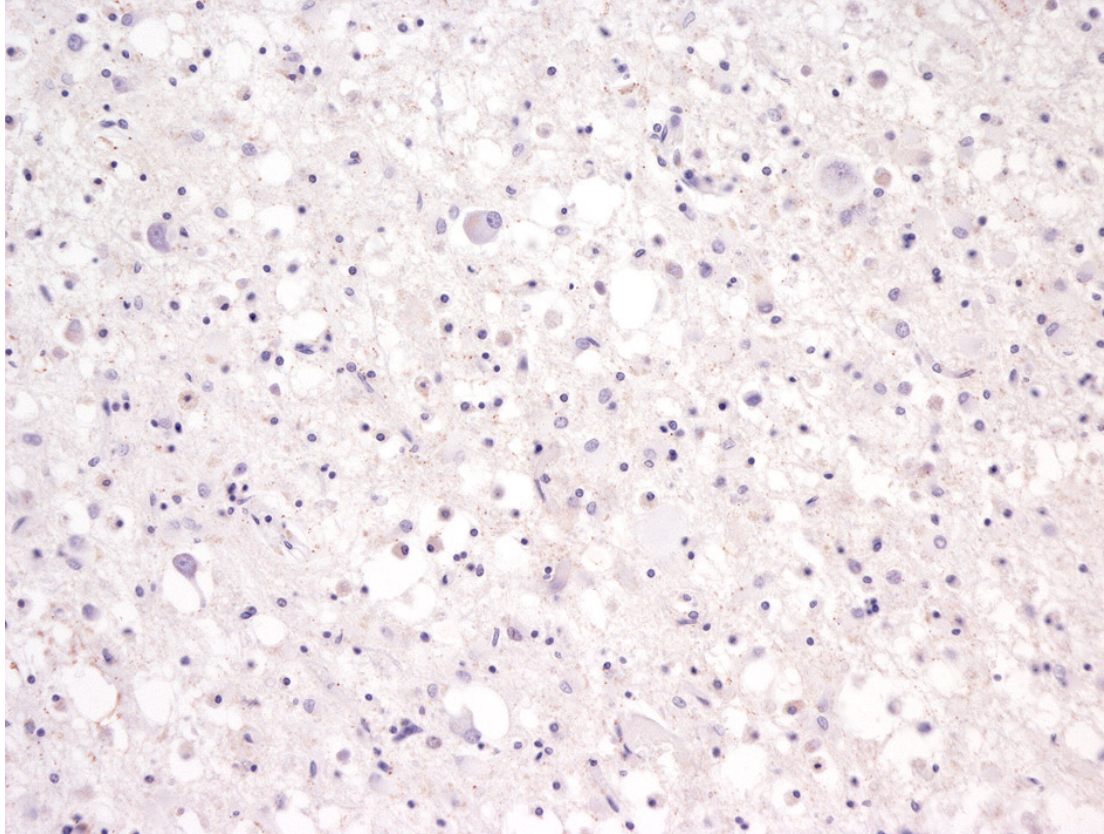
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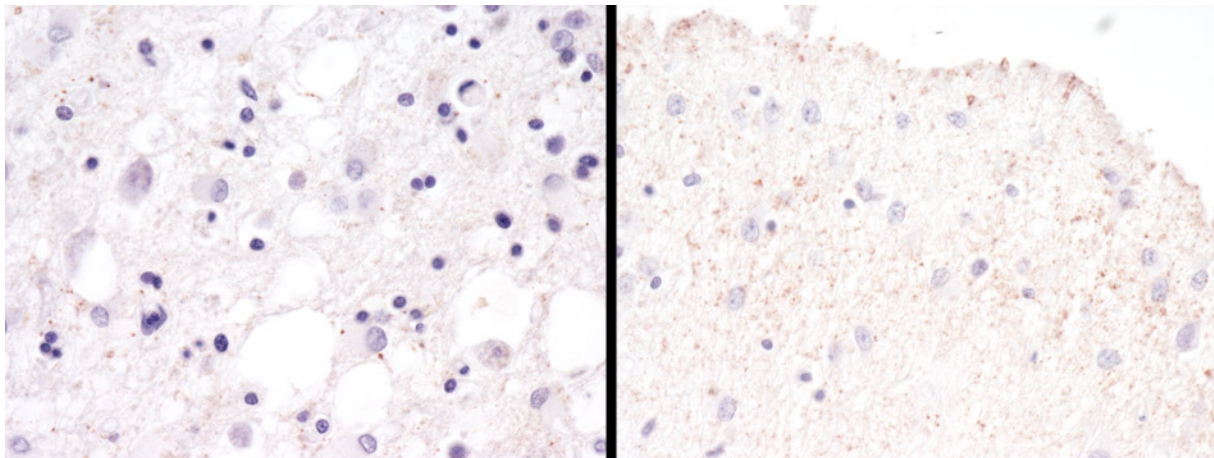
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**Case 5:** Cx43 does not show enhanced immunoreactivity in reactive astrocytes (magnification: x200).



In the same case, the enlarged image of a reactive astrocyte (left side of image) lack prominent Cx43 immunoreactivity, but subpial astrocytes (right side of image) show physiological strong immunoreactivity.



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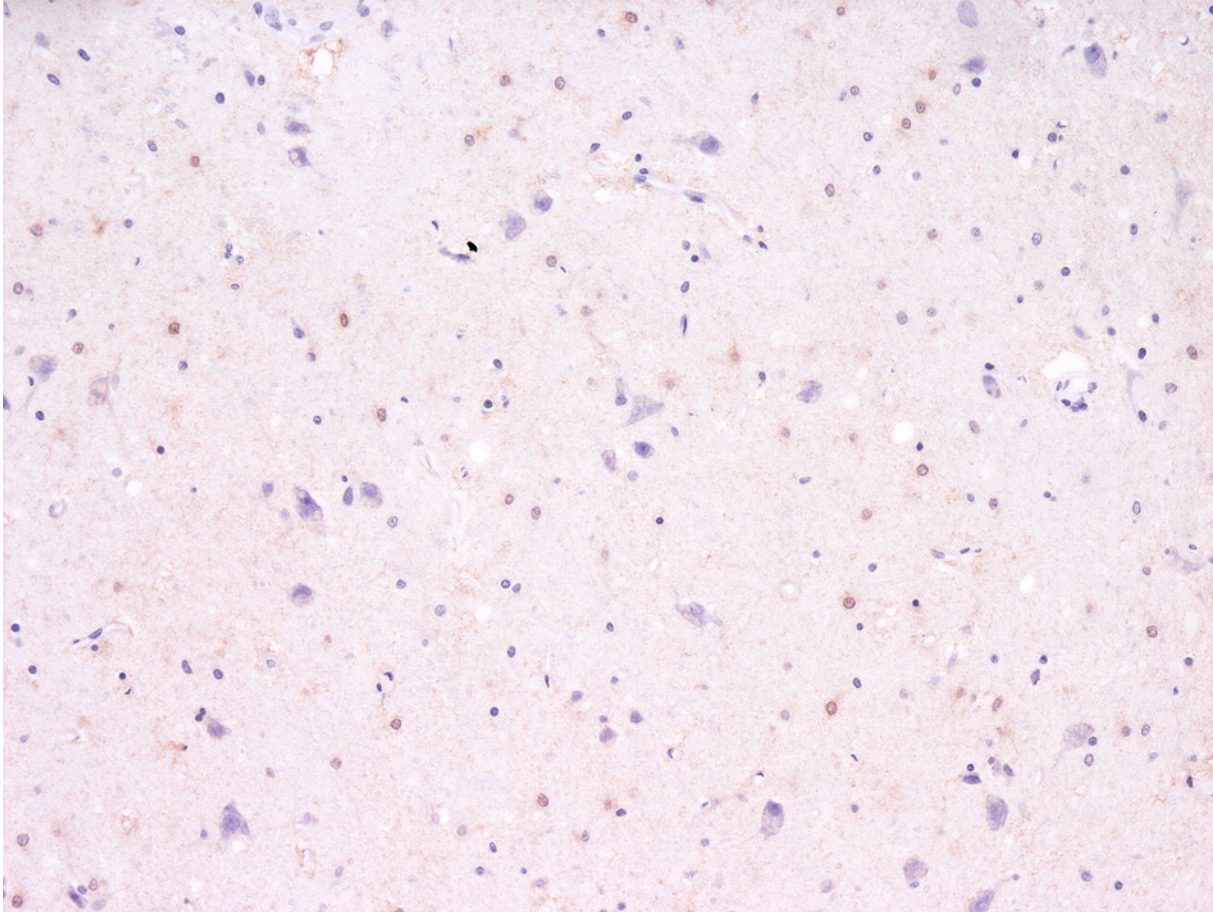
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**Case 6:** Cx43 does not show enhanced immunoreactivity in reactive astrocytes (magnification: x200).



### **Conclusion:**

Increased Cx43 immunoreactivity is not due to pure reactive astrogliosis. We conclude that in ARTAG the increased Cx43 density of immunoreactivity is most likely associated with further pathogenic events.