**S1 Table.**

Reported premorbid conditions and neuropathology associated with AstV-ND in humans and animals.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Underlying disease** | **Infected CNS regions/CSF** | **Infected**  **cells** | **Diagnosis and neuropathological findingsa** | **Outcome of AstV-ND (n)b** | **Reference** |
| **Humans** |  |  |  |  |  |
| X-linked agamma- globulinemia | Brainstem, cerebellum,  frontal cortex,  basal ganglia | Astrocytes  Neurons | Encephalitis: Astrocytosis (GFAP); microgliosis (CD68); T-cell perivascular/parenchymal infiltration (CD3); neuronal loss; axonal swelling; myelin degeneration | Fatal (1) | Quan et al, 2010 [[1](#_ENREF_1)]c |
| Severe primary combined immunodeficiency | Brainstem, cerebellum,  basal ganglia, hippocampus | NR | Meningoencephalitis: Leptomeningeal/ periventricular inflammatory cell infiltration; necrosis; inflammatory cells not phenotyped | Fatal (1) | Wunderli et al, 2011 [[2](#_ENREF_2)] |
| Chronic lymphocytic leukemia | Frontal cortex | Neurons | Encephalitis: Astrocytosis (GFAP); microgliosis (CD68); T-cell parenchymal infiltration (CD3) | Fatal (1) | Naccache et al, 2015 [[3](#_ENREF_3)]c |
| X-linked agamma-globulinemia | Frontal cortex | NR | Encephalitis: Microgliosis (IBA1); T-cell peri-vascular /parenchymal infiltration (CD3/CD8) | Recovery (1) | Fremond et al, 2015 [[4](#_ENREF_4)]c |
| Cartilage hair hypoplasia | Cerebral cortex | Neurons | Encephalitis: Astrocytosis (GFAP); microgliosis (CD68); T-cell minimal infiltration (CD3);  neuronal apoptosis | Fatal (1) | Brown et al, 2015 [[5](#_ENREF_5)]c |
| Acute myeloid leukemia | Unspecified | NR | Encephalitis: Hypercellularity; perivascular/ leptomenin-geal inflammatory cell infiltration; inflammatory cells not phenotyped | Fatal (1) | Lum et al, 2016 [[6](#_ENREF_6)]c |
| Acute myeloid leukemia | Hypothalamic region | NR | Encephalitis: Myelin breakdown and neuronal microvesicular inclusions | Recovery (1) | Krol al, 2021 [[7](#_ENREF_7)] c |
| Acute myeloid leukemia | CSF | NR | Meningitis: NR | Fatal (1) | Cordey et al, 2016 [[8](#_ENREF_8)] |
| Congenital aplastic anemia | CSF | NR | Encephalopathy: NR | Recovery (1) | Sato et al, 2016 [[9](#_ENREF_9)] |
| None | CSF | NR | Meningitis NR | Recovery (1) | Cordey et al, 2016 [[8](#_ENREF_8)] |
| None | CSF | NR | Encephalitis: NR | Recovery (1) | Koukou et al, 2019 [[10](#_ENREF_10)] |
| None | CSF | NR | Meningitis: NR | Unknown (1) | Wilson et al, 2019 [[11](#_ENREF_11)] |
| B-cell acute lympho- blastic leukemia | CSF | NR | Encephalitis: NR | Recovery (1) | Bami et al, 2022 [[12](#_ENREF_12)] c |
| Acute myeloid leukemia | CSF | NR | Encephalitis: NR | Fatal (1) | Bami et al, 2022 [[12](#_ENREF_12)] c |
| **Cattle** |  |  |  |  |  |
| Unknown | Cerebellum, brainstem,  spinal cord, thalamus,  basal ganglia, cerebral cortex | Neurons | Neuronal degeneration; microgliosis; astrocytosis; perivascular infiltration (lymphocytes, macrophages, and plasma cells); inflammatory cells not phenotyped | Euthanasia | Li et al, 2013 [[13](#_ENREF_13)] |
| Unknown | Brainstem, cerebellum,  cerebrum | Neurons | Degeneration of neurons; microgliosis; perivascular infiltration; inflammatory cells not phenotyped | Euthanasia | Selimovic-Hamza et al, 2016, 1017 [[14](#_ENREF_14), [15](#_ENREF_15)] |
| Unknown | Medulla | Neurons | Degeneration of neurons; microgliosis;  inflammatory cells not phenotyped | Euthanasia | Bouzalas at, 2014 [[16](#_ENREF_16)] |
| **Pigs** |  |  |  |  |  |
| Unknown | Spinal cord, brainstem,  cerebellum, cerebral cortex | Neurons | Degeneration of neurons; microgliosis; perivascular/leptomeningeal infiltration;  inflammatory cells not phenotyped | Euthanasia | Boros et al. 2017 [[17](#_ENREF_17)] |
| **Sheep** |  |  |  |  |  |
| Unknown | Cerebellum, spinal cord, cerebrum | NR | NR | Euthanasia | Pfaff et al. 2016 [[18](#_ENREF_18)] |
| **Muskox** |  |  |  |  |  |
| Unknown | Spinal cord, midbrain | Unspecified | Perivascular cuffs; neuronal degeneration; gliosis; inflammatory cells not phenotyped | Euthanasia | Boujon et al, 2019 [[19](#_ENREF_19)] |
| **Alpaca** |  |  |  |  |  |
| Unknown | Spinal cord, brainstem,  cerebellum, thalamus,  cerebral cortex, hippocampus | Neurons | Predominantly lymphocytic perivascular cuffs; neuronal degeneration; gliosis; axonal degeneration, inflammatory cells not phenotyped | Euthanasia | Küchler et al, 2021 [[20](#_ENREF_20)] |
| **Mink** |  |  |  |  |  |
| Unknown | Unspecified | NR | NR | Euthanasia | Blomstrom et al, 2010 [[21](#_ENREF_21)] |

a Neuropathological findings in humans are reported from postmortem or biopsy brain tissue samples in fatal or recovery cases, respectively. b Number of reported AstV-ND cases in humans. c Genotype of the astrovirus causing infection of the human CNS: Human VA1 clade. NR, not reported.

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