

Table 1: Timeline of clinical progress and key investigations.

Clinical progress	Key investigations
<ul style="list-style-type: none"> • Day 0: symptom onset with fever and vomiting. • Day 2: difficulty swallowing food. • Day 3: difficulty drinking liquids. Medical attention sought: “For some reason, his throat rejects foods and even water. It’s like a gag reflex”. Admitted to Whangārei Hospital. • Day 4: onset of agitation and paranoid ideation. Hydrophobia and oxygen therapy intolerance (possible aerophobia). Intubated and transferred to ICU due to agitation. Empirical meningoencephalitis treatment started (ceftriaxone, clarithromycin and aciclovir). • Day 5: transferred to Auckland City Hospital ICU. Autonomic dysfunction with abnormal respiration and tachycardia interspersed with bradycardia. Benzylpenicillin and doxycycline added to antimicrobial regimen. • Day 6: ongoing fevers and autonomic dysfunction with marked hypoxia requiring deep sedation. Abnormal gagging motions, eye rolling and neck flexion movements noted, levetiracetam added. • Day 7: progressive haemodynamic instability and challenging mechanical ventilation with echocardiography showing severely globally impaired LV. Abnormal jaw and pharyngeal movements. Methylprednisolone IV commenced for possible autoimmune encephalitis (5-day course). • Day 12: antimicrobials stopped. • Day 14: hypersalivation noted (over 1L/day saliva losses). Sedation progressively weaned. • Day 15: resolving autonomic instability. • Day 17: pupils unreactive. • Day 19: absent cough reflex, oculocephalic reflex and deep tendon reflexes, with intact corneal reflexes. Repeat rabies serology positive, demonstrating IgG seroconversion to rabies virus. 	<ul style="list-style-type: none"> • Days 3–8 <ul style="list-style-type: none"> • Admission bloods: white cell count $22.5 \times 10^9/L$ (normal range 4–11), neutrophils $19.6 \times 10^9/L$ (1.9–7.5), lymphocytes $0.9 \times 10^9/L$ (1–4), HbA1c mmol/mol 77 (<41), C-reactive protein 2 mg/L (0–5), renal and liver function grossly normal. • Cerebrospinal fluid (CSF) analysis: protein 0.39 g/L (0.15–0.45), glucose 7 mmol/L (2.8–4.4), white cell count $14 \times 10^6/L$, neutrophils 1%, monocytes 9%, lymphocytes 90%, CSF PCR panel negative for common viral and bacterial causes of community-acquired meningoencephalitis, bacterial culture no growth, <i>Mycobacterium tuberculosis</i> culture no growth after 6 weeks. • Blood cultures and urine culture no growth. • Infectious serology: HIV, syphilis, EBV, CMV, HAV, HBV, HCV, <i>Rickettsia</i>, cryptococcal antigen not consistent with recent or acute infection. • Respiratory virus PCR panel and atypical pneumonia PCR panel negative, <i>Legionella</i> urinary antigen negative. • Malaria blood films negative, flavivirus PCR of urine and serum negative, <i>Leptospira</i> PCR on urine negative. • Autoimmune serology: ANCA and ANA screen negative, anti-neuronal antibodies in serum and CSF negative. • Imaging: chest X-ray no abnormalities detected, CT head, chest and abdomen non-significant, initial MRI brain (day 5) grossly normal, TTE: globally impaired LV systolic function (LVEF 29%). • Day 8: <i>Lyssavirus</i> genus PCR on urine, serum and CSF negative. • Day 10: initial rabies serology (IgG) negative.

Table 1 (continued): Timeline of clinical progress and key investigations.

<ul style="list-style-type: none">• Day 20: Lyssavirus genus detected by polymerase chain reaction (PCR) in saliva and nape of neck skin biopsy specimens, consistent with rabies virus but species to be confirmed.• Day 21: loss of respiratory drive, onset of diabetes insipidus.• Day 23: absent motor responses and cranial nerve reflexes. Family meeting to discuss withdrawal of intensive care supports, and then palliatively extubated in presence of family. Death confirmed 10 minutes post-extubation.	<ul style="list-style-type: none">• Day 15: repeat rabies serology (IgG) positive (resulted day 19).• Days 16–17: Lyssavirus genus PCR on saliva x3 and nape of neck skin biopsy positive, Australian bat lyssavirus (ABLV) negative (resulted day 20)—later confirmed as rabies virus by sequencing, consistent with virus of Philippines origin.• Day 21: MRI brain—repeat MRI showing progressive changes as detailed in Figure 1.
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Figure 1: Magnetic resonance imaging (MRI) brain images from the patient.

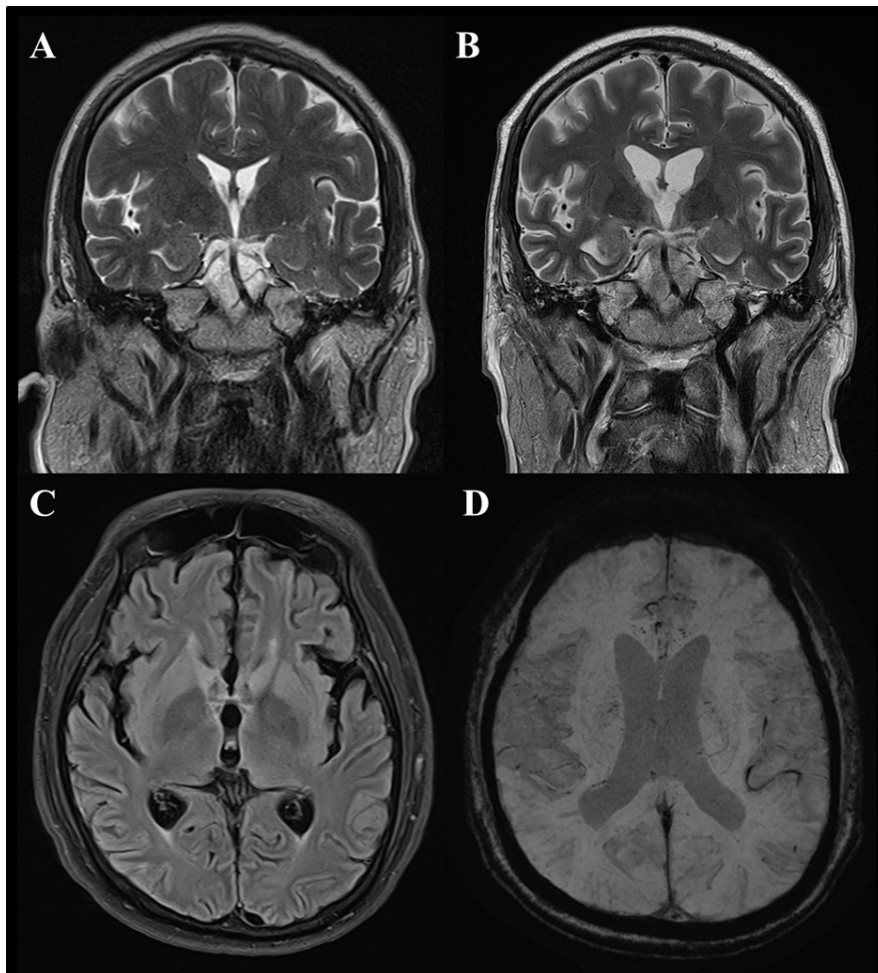


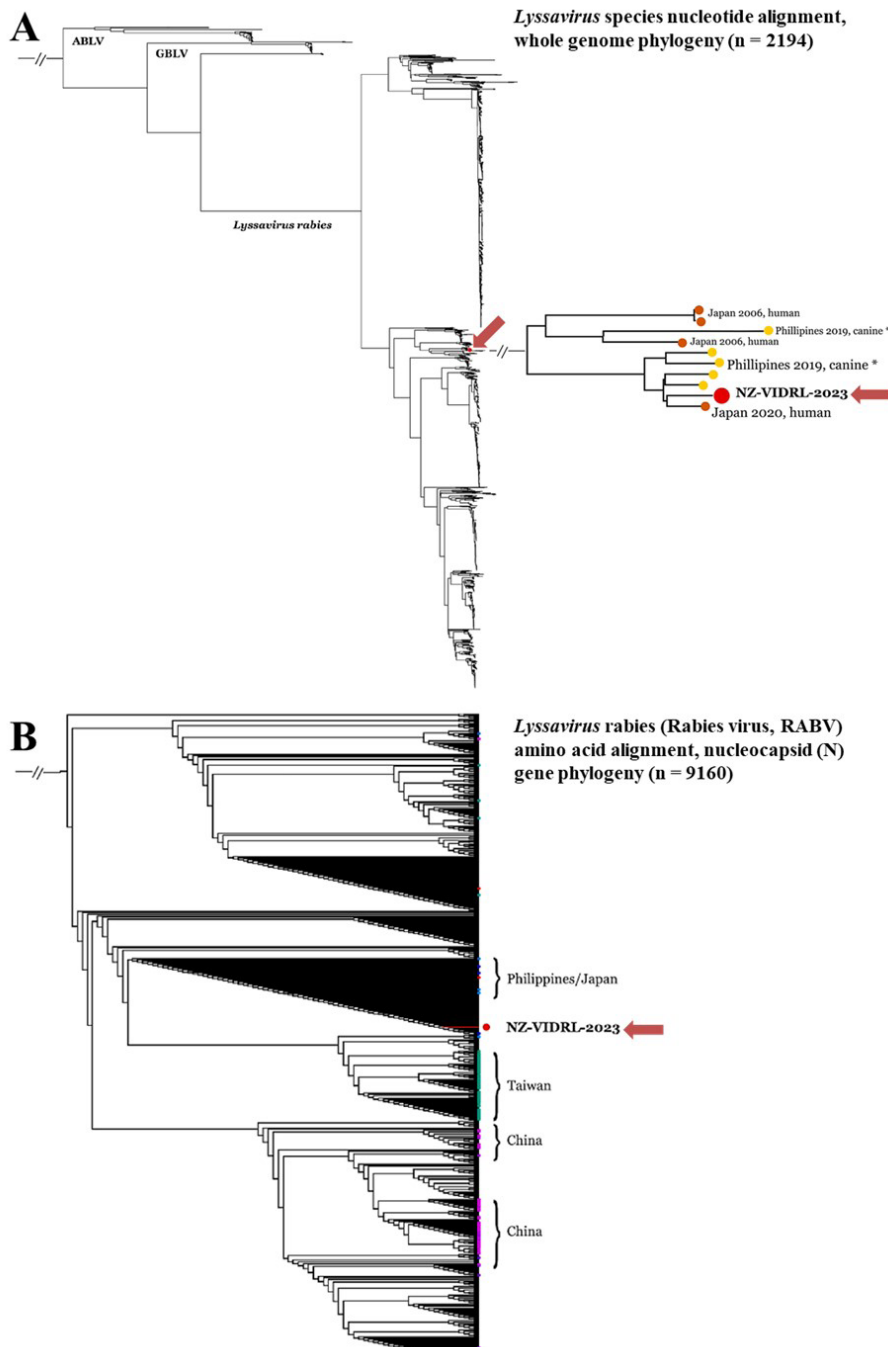
Figure 1a) Day 5 MRI identified no significant abnormalities.

Figure 1b) Day 21 MRI demonstrated cerebral volume loss with widening of sulcal spaces and increased ventricular size when compared to day 5 MRI.

Figure 1c) Day 21 MRI fluid attenuation recovery (FLAIR) sequence showing mild diffuse increased signal in the cerebral cortex and caudate head, globus pallidus and hypothalamus.

Figure 1d) Day 21 MRI susceptibility weighted imaging (SWI) demonstrating small hypointense foci on at the genu of the corpus callosum consistent with microhaemorrhages. Such changes are described in the literature.⁴

Figure 2: Whole genome phylogenetic tree (a) and N-gene cladogram (b) for the rabies virus isolated from our patient (marked with red dots annotated “NZ-VIDRL-2023” and indicated by red arrows).



The detected *Lyssavirus* was confirmed as RABV, with nucleoprotein (N) gene Sanger sequencing yielding a 100% match to GenBank LC752966.1 *Lyssavirus rabies* 0512 N-gene, and whole genome sequencing of the detected virus giving 100% coverage with GenBank LC619707 Toyohashi strain RABV (also isolated from a Filipino patient, marked with an orange dot annotated “Japan 2020, human”).⁵

Note that while the virus detected from this patient is shown as being closely phylogenetically related to RABV strains from Japan and the Philippines, rabies was eliminated from Japan in 1957⁵ but remains highly endemic in the Philippines, which has approximately 200–300 human cases annually.⁶ The three recent cases diagnosed in Japan in 2006 and 2020 (marked with orange dots) were all acquired in the Philippines, reflecting the common geographic origin of this cluster in the phylogenetic tree.⁵

Key: ABLV, Australian bat lyssavirus (*Lyssavirus australis*); GBLV, Gannoruwa bat lyssavirus (*Lyssavirus gannoruwa*).