

A case of imported rabies in Aotearoa New Zealand

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Rabies is a zoonotic encephalitis caused by viral species within the *Lyssavirus* genus.¹ Rabies virus (RABV; species *Lyssavirus rabies*) transmitted from dog bites is the most common cause of human rabies.¹ Rabies is not endemic in Aotearoa New Zealand,² and here we describe Aotearoa New Zealand's first recorded case.³

Case report

A 48-year-old Filipino man presented to hospital with fever, vomiting and inability to swallow food or fluids (day 3 post-symptom onset). There was no history of an animal bite from the patient (while lucid), or his wife. He worked on a commercial cargo ship and had not disembarked since boarding in the Philippines over 7 months earlier. There were reportedly no animals on board. He had a background of type 2 diabetes mellitus, for which he took metformin and gliclazide.

On examination on the day of presentation (day 3 of illness), he was febrile (38.6°C) and anxious. Initial blood tests showed a neutrophilia and normal C-reactive protein. On day 4 he became increasingly agitated and paranoid, necessitating sedation and intubation for ongoing management. Initial CT and MRI brain imaging were unremarkable (Figure 1). CSF analysis demonstrated a lymphocytic pleocytosis. Routine CSF microbiological investigations and autoimmune encephalitis screen were negative. He received empirical broad-spectrum antimicrobials to cover bacterial meningitis and viral encephalitis, and a 5-day course of methylprednisolone (1g/day) for a possible autoimmune cause. On day 5 he developed significant autonomic instability with alternating tachypnoea and apnoea, and episodes of extreme hypertension interspersed with hypotension.

Urine, serum and CSF collected on day 8 were tested with a pan-*Lyssavirus* genus reverse transcription real-time PCR, which was negative. Day 10 serum was negative for RABV IgG. The patient became progressively obtunded from day 14, with marked hypersalivation (saliva losses exceeding 1L/day). Day 15 serum demonstrated

RABV IgG seroconversion. Three saliva samples and a nuchal (nape of neck) skin biopsy collected on days 16–17 all tested positive for *Lyssavirus* genus RNA by PCR. The detected *Lyssavirus* was confirmed as RABV by sequencing (Figure 2). His obtundation progressed to absent respiratory drive and multi-organ failure, and he died on day 23 post-symptom onset. The patient was managed with infection prevention and control (IPC) standard precautions, with appropriate personal protective equipment (PPE) used when staff were at risk of contact with infectious bodily fluids.

Discussion

When RABV from saliva of an infected animal contacts non-intact skin (via a bite), it enters peripheral motor nerves and travels to the spinal cord (typical incubation period ~20–90 days).¹ Dorsal root ganglia infection produces inflammation, leading to fever, pruritus and paraesthesia (prodromal phase, ~1–2 days).¹ From the spinal cord, RABV rapidly disseminates within the central nervous system (CNS) to produce an acute neurological phase (~1–4 days) with an encephalitic (agitation, hypersalivation, hydrophobia and autonomic dysfunction) or paralytic clinical picture (muscle weakness, paralysis and drowsiness).¹ Development of symptoms is almost invariably followed by death within 1–2 weeks, which may be extended by ICU care.¹

Following CNS dissemination, the virus spreads outwards via parasympathetic nerves to multiple sites, including skin sensory nerves and salivary glands to facilitate onwards transmission via saliva.¹ Optimal ante-mortem investigations reflect this pathophysiology: saliva specimens (containing excreted virus) and a nuchal skin biopsy (skin nerves close to the CNS) for PCR testing.¹ Our patient evidently lacked prior immunity from rabies immunisation, making paired serology useful in this case for demonstrating RABV IgG seroconversion. Within Aotearoa New Zealand, rabies serology is currently available through Awanui Labs (formerly Labtests), Auckland and Canterbury Health Laboratories, Christchurch.^{7,8}

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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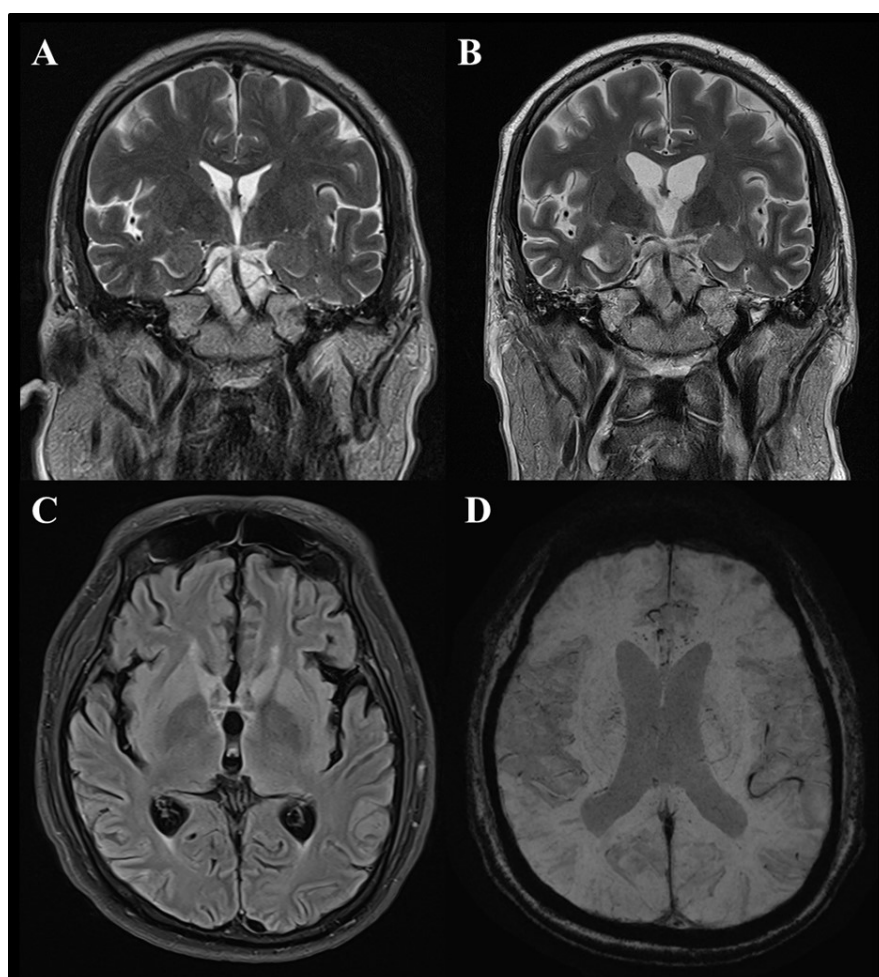
Figure 1: Magnetic resonance imaging (MRI) brain images from the patient.

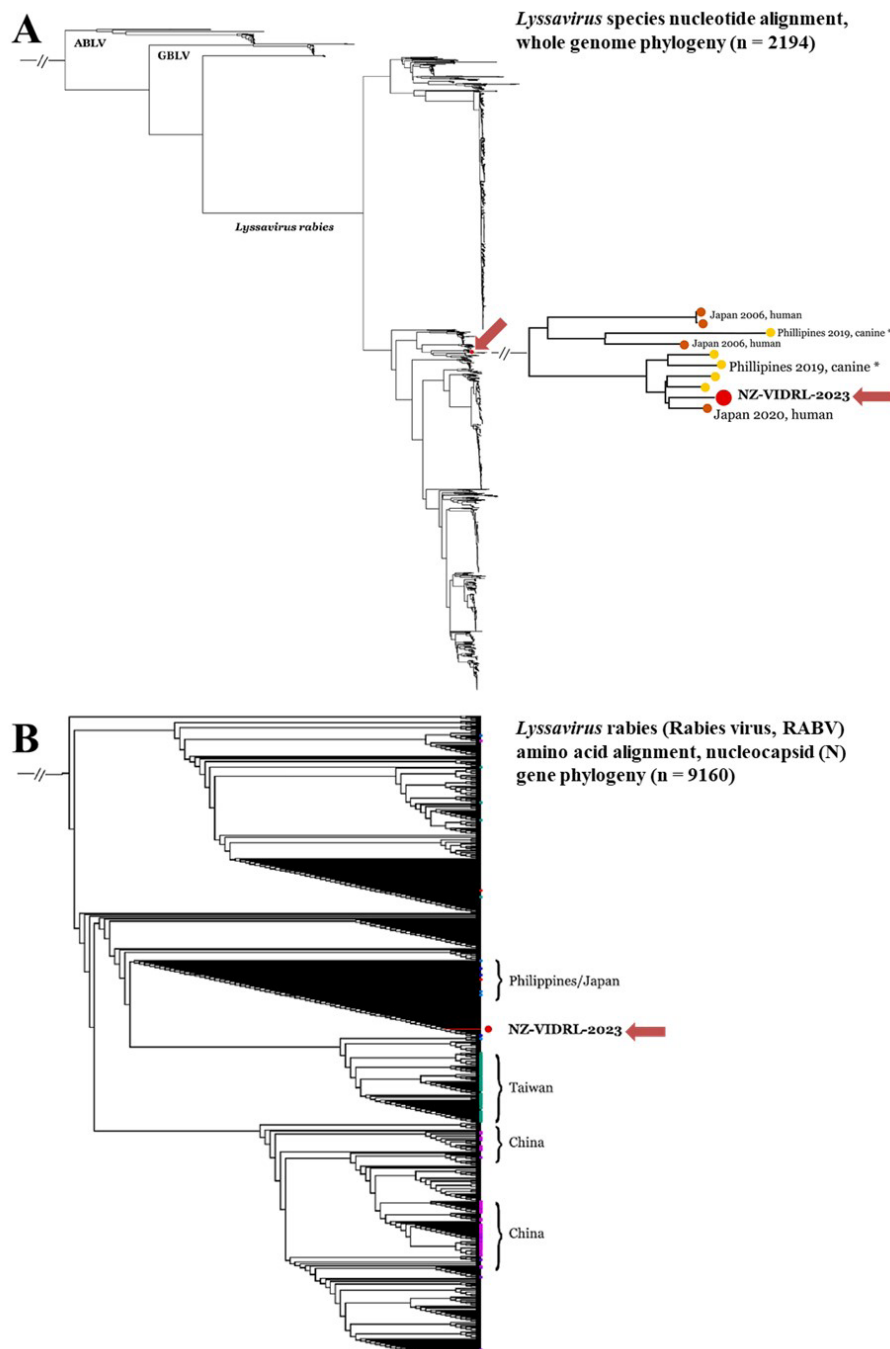
Figure 1a) Day 5 MRI identified no significant abnormalities.

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 attenuated inversion 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*).

Rabies PCR testing is not currently available in Aotearoa New Zealand and can be referred to the Victorian Infectious Diseases Reference Laboratory (VIDRL) in Melbourne, Australia.⁹

The patient developed symptoms after 7 months at sea without shore leave. As demonstrated by this case, the long incubation period, which can extend for several years in rare cases,¹⁰ makes eliciting an animal bite history challenging. This means compatible symptoms and prior travel to a rabies endemic area may be the only clues to the diagnosis. Rabies is highly endemic in the Philippines,⁶ and our patient was likely infected there before embarking.

Rabies is transmitted when infectious bodily fluids (saliva, tears, respiratory secretions) or CNS tissue comes into direct contact with non-intact skin or mucous membranes (eyes, nose or mouth).¹¹ Blood, urine and faeces are deemed non-infectious, and rabies cannot be transmitted via objects/surfaces.¹¹ Standard precautions should be used for care of all patients,¹² and are

considered appropriate for the care of patients with suspected or confirmed rabies.^{2,11} This means that staff that are likely to come into contact with infectious bodily fluids should wear gowns, goggles, masks and gloves, particularly when performing activities such as intubation and suctioning.¹¹ Post-exposure prophylaxis is only warranted following a direct exposure as described above, or when a contact has been bitten by a case.² Care of a patient with suspected or confirmed rabies can generate anxiety among attending healthcare workers, especially in non-endemic settings. Anxiety can be managed through staff education regarding which bodily fluids are infectious, reinforcing the value of correct standard precautions for all patients and reassurance that standard precautions are effective in preventing rabies transmission and that there has never been a case of human-to-human rabies transmission from a patient to a healthcare worker (human-to-human transmission has only occurred in the setting of organ/tissue transplantation).¹¹

COMPETING INTERESTS

Nil.

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