A DIFFICULT CASE

The Story

A right-handed conservationist in his fifties, who was also an artist and licensed bat handler, was admitted to hospital with a history of acute painless haematemesis. He also complained of severe pain in his left arm and shoulder over the preceding 7 days for which he had been taking ibuprofen without much benefit. Past medical history included pulmonary tuberculosis in childhood. He was otherwise well. There was no family history of note.

He had not been abroad in the previous 7 years, and had been resident in Angus, Scotland, for 3 years, working with Scottish National Heritage. He was able to give a history of bat contact, indeed he had been bitten by a Daubenton’s bat (Fig. 1) on his left hand 4 months prior to admission. He had never in the past received any anti-rabies vaccine nor had he received any post-exposure anti-rabies prophylaxis.
ON EXAMINATION
He was pyrexial (38.5 °C) but haemodynamically stable. He appeared euphoric and disinhibited, but was alert and fully orientated. Apart from a slightly diminished gag reflex his cranial nerves were normal. Tone and power in the limbs were normal. There were no deep tendon reflexes in his arms, he had brisk reflexes in the lower limbs and the plantar responses were bilaterally extensor. He had patchy numbness to pinprick over the left upper limb. He had mild gait ataxia.

THE TESTS
Investigations revealed a neutrophilia of 18 × 10⁹ (total white blood cell count 25 × 10⁹), but normal blood biochemistry. His chest X-ray revealed right lower zone consolidation. The clinical impression at this stage was ‘acute encephalomyelitis of probable inflammatory or infective aetiology’.

He had an urgent CT scan of his head, which was normal and a subsequent MR scan was also normal, but MRI of the cervical spine showed abnormal increased signal intensity in the spinal cord at C7 on T2-weighted images (Fig. 2). The significance of this was uncertain. His CSF revealed a mildly elevated protein (585 mg/L), normal glucose and no cells. There were no organisms on gram staining, or any acid fast bacilli. Subsequent blood and CSF cultures were negative and blood serology for atypical infections were also negative.

At this stage rabies encephalitis was considered in view of the encephalopathy with progressive paralysis, and the history of bat bite in the potential incubation period. Saliva and skin biopsy samples (from nape of neck and the bat bite site) were sent to the Veterinary Laboratories Agency, Weybridge, for rabies PCR tests. Repeat CSF samples were also sent for rabies PCR.

PROGRESS
He continued to deteriorate, his upper limbs became weak and he lost the reflexes in both lower limbs. He also appeared emotionally labile and agitated at times. On day six of admission he rapidly became very unwell. He was confused, agitated and appeared encephalopathic. He was generally flaccid, weak and areflexic. He had developed collapse-consolidation of his right lung and was hypoxic. He was transferred to ITU for ventilatory support. He was treated with IV immunoglobulin in view of the possible diagnosis of atypical ‘acute inflammatory demyelinating polyneuropathy’. The CSF, skin biopsy and first saliva samples were negative for rabies, and further saliva samples were sent for rabies PCR.

By day eight he was off any sedation and deeply comatose. His EMG and nerve conduction studies revealed normal conduction velocities in peripheral nerves, reduced compound muscle action potentials and relatively spared sensory responses suggesting loss of motor axons predominantly. His EEG revealed very slow background activity interspersed with runs of intermediate slow waves (Fig. 3).

While PCR results on further saliva samples were awaited his autoantibody screen revealed elevated IgM anticardiolipin antibody and anti dsDNA antibodies and so a possible vasculitic aetiology was considered. Multiple venous blood samples sent for rabies antibody were negative. But, on day 10, further saliva samples tested conclusively positive for rabies virus EBL2a by partial sequencing of PCR products.

On day 14 his artificial life support was withdrawn at the request of his family.

During his stay in the ITU he had been quarantined and contact with health personnel kept to the minimum necessary. He had been nursed using universal precautions. All the individuals who had come in close contact with him were offered post exposure rabies vaccination.

THE POST MORTEM
External examination of the body was unremarkable. The internal organs showed no pre-existing disease. The oesophagus had patchy mucosal congestion confirmed as oesophagitis and this was thought to be responsible for the
presentation with haematemesis. There was also mild haemorrhagic gastritis. The heart appeared normal but on microscopy there was evidence of terminal heart failure with congestion and oedema of the lungs, small pleural effusions and early chronic passive congestive changes in the liver. The brain and spinal cord were not swollen and appeared normal to the naked eye. Skeletal muscle texture was flabby given the state of rigor mortis and microscopically showed signs of denervation. Microscopic examination of the brain and spinal cord showed a florid rabies-like pan-encephalomyelitis. The cervical spinal cord lesion seen on imaging proved to be an area of more severe myelitis.

The diagnosis was confirmed by FAT (fluorescent antibody test), and by viral isolation on three brain samples – cerebellum, medulla and hippocampus (Table 1). Also, Rt-PCR on these tissues was positive for rabies, confirmed by sequencing as EBLV-2. In addition to this, mouse inoculation tests revealed a rabies-like illness between 13 and 17 days post infection and mouse brain smears were positive by FAT.

**DISCUSSION**

Worldwide around 50,000 people die of rabies every year, mainly in the developing world. Owing to our stringent animal quarantine policy, rabies surveillance and post exposure prophylaxis, the UK is and has been a rabies free country for the last 100 years – the previous indigenously acquired case was reported in 1902. And between 1977 and 2000 there have only been nine deaths due to rabies, all acquired outside the UK.

The European bat lyssavirus (EBLV) is a rabies-like virus from the rhabdovirus family (lyssavirus genotype 5 & 6). It is carried by European insectivorous bats. EBLV infection has rarely been reported in humans and there have been only three reported deaths in Europe. None of
these three patients had received any post-exposure rabies prophylaxis. Although the vaccine is based on the common rabies virus (genotype 1), there is a cross immunity with genotype 5 and 6 and it is highly effective.

Between 1977 and 2000, 630 cases of EBL infection in bats were reported in Europe. In the UK, bats have been screened for Lyssavirus infection since 1985. Out of 3000 bats tested so far (1987–2002) only 35 were Daubenton’s bats (myotis daubentonii) and only two were found to have European bat lyssa virus infection, both were Daubenton’s bats. From genetic analysis one of these two bats was traced as coming from the Swiss-French border.

In the UK bats are a protected species. They are mostly fruit eating and insectivorous and play a vital role in maintaining environmental balance. There are about 92 bat conservation societies in the UK with more than 3000 licensed bat handlers working with them. Daubenton’s bats favour a riverside habitat and tend to avoid human contact. While the general population is not at risk from them because of limited contact, bat handlers are. Advice regarding bats in the UK changed following a case of bat rabies in Lancashire in 2002 – only licensed or volunteer bat handlers should routinely come into contact with bats, and take care and wear bite-proof gloves. The Department of Health advice is that all bat handlers whether licensed or not should be vaccinated preventively. Vaccine is provided free-of-charge to all bat handlers by the Health Protection Agency (formally the Public Health Laboratory Service).

Our case has led to a change in policy for the management of people who have had close exposure to bats in the UK. Prophylaxis for exposure to EBL is the same as that recommended for all potential rabies virus exposures and appears to be highly effective. Anyone who has been scratched or bitten by a UK bat, or whose eyes, broken skin or mucous membrane has come into contact with bat saliva or neural tissue from a UK bat, should be offered post-exposure vaccination as soon as possible after the incident. If the person is already fully immunized against rabies, they should be offered two doses of vaccine. If they are previously non-immune or incompletely immunized, they should be offered five doses. For those who are previously non-immune and who have been bitten by a bat that is known, or strongly suspected, to be rabid, then immunoglobulin may be offered in addition to a full course of vaccine. Public health authorities in all other countries should note the change of policy so that returning travellers who report exposure to bats in the UK are offered prophylaxis if appropriate.

The risk of bat rabies infection to humans is extremely low, less than winning the national lottery or being hit by lightning. This is reflected in the definitions of ‘rabies-free’ zones given by the WHO and the International Office of Epizootics, in that bat rabies does not count as a rabies-infected zone. Hence although this case will not affect the United Kingdom’s rabies free zone status, it reminds us that rabies can still present as an unusual acute neurological illness, even in Scotland.

### Table 1 Post-mortem testing for rabies

<table>
<thead>
<tr>
<th>TEST SPECIMEN</th>
<th>FIRST ROUND RABIES PCR</th>
<th>SECOND ROUND RABIES PCR</th>
<th>FLUORESCENT ANTIBODY TEST FOR RABIES</th>
<th>MOUSE INOCULATION TEST FOR RABIES</th>
<th>RABIES VIRUS ISOLATION</th>
</tr>
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<tbody>
<tr>
<td>Cerebellum</td>
<td>+</td>
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<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Medulla</td>
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<td>+</td>
<td>+</td>
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<tr>
<td>Hippocampus</td>
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<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Submandibular salivary gland</td>
<td>–</td>
<td>+</td>
<td>+/–</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>Parotid gland</td>
<td>–</td>
<td>+</td>
<td>+/–</td>
<td>Not done</td>
<td>Not done</td>
</tr>
</tbody>
</table>

### FURTHER READING