# Appendix 1:

## Table 1: Important paraneoplastic neurologic syndromes

<table>
<thead>
<tr>
<th>Brain</th>
<th>Spinal Cord</th>
<th>Peripheral Nerves</th>
<th>Neuromuscular Junction</th>
<th>Muscles</th>
<th>Retina</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limbic Encephalitis</td>
<td>Paraneoplastic necrotizing myelopathy</td>
<td>Sensory neuropathy</td>
<td>Lambert-Eaton syndrome</td>
<td>Dermatomyositis &amp; Polymyositis</td>
<td>Cancer associated retinopathy</td>
</tr>
<tr>
<td>Brainstem encephalitis</td>
<td>Inflammatory Myelopathy</td>
<td>Motor neuropathy</td>
<td>Myasthenia gravis</td>
<td>Necrotizing myopathy</td>
<td>Optic neuritis</td>
</tr>
<tr>
<td>Cerebellar degeneration</td>
<td>Stiff person syndrome</td>
<td>Mixed sensory motor neuropathy</td>
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<tr>
<td>Opsoclonus-Myoclonus</td>
<td>Mononeuritis multiplex</td>
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<tr>
<td>Chorea</td>
<td>Autonomic neuropathy</td>
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</tbody>
</table>
Appendix 2:

Investigations:

The contrast-enhanced CT head scans of patients with limbic encephalitis may be normal, yet the cranial MRI may show distinctive features [28]. The MRI brain scans in patients with limbic encephalitis often suggest relatively widespread changes in the brain parenchyma. The T2 signal is increased in the temporal lobes and often also in the cortex and brainstem [23, 29]. In a recent study, twenty-five of 44 (57%) patients with LE had signal abnormalities in the limbic system on MRI brain [3]. In our patient, CT brain did not reveal any abnormality. A number of small high signal foci were seen in the white matter on T2 weighted images of MRI. They were reported as ischaemic changes. There are published reports on cerebellar degeneration associated with paraneoplastic LE [30]. Our patient had an ataxic gait but did not have other signs of a cerebellar involvement.

The EEG may show epileptic activity with focal slowing and/or paroxysmal sharp waves and spikes in the temporal lobes and hippocampal regions [3,23]. EEG recordings in our patient were abnormal with excessive bilateral slow wave activity without any lateralisation or localising features. There were no epileptic features. The positron emission tomographic scans may demonstrate hippocampal hypermetabolism and this may indicate subclinical seizure activity [31]. The CSF examination often shows elevated protein levels, mild mononuclear pleocytosis, oligoclonal bands, or increased IgG levels but may be normal [2]. The CSF was unremarkable in our patient except for mild protein elevation.
The pathological examination usually shows a patchy and multifocal neuronal loss with perivascular infiltration by lymphocytes and gliosis in the hippocampus, amygdala, and cingulate and frontal cortex [2, 32-34].

**Diagnosis:**

Diagnosis of LE is almost certain in the presence of an underlying malignancy, relevant clinical presentation and serum or CSF antineuronal antibodies. However, limbic encephalitis can be misdiagnosed as a vascular or Lewy body dementia. Differential diagnosis also includes an infection of the brain parenchyma. This was excluded in our patient by a normal CSF analysis and negative tests for herpes simplex, varicella zoster, entero virus, syphilis, toxoplasma, chlamydia, brucella and legionnaire’s disease. Systemic lupus erythematosus and other connective tissue diseases were excluded by the negative autoantibody tests. The pattern of the illness was not consistent with a vascular pathology. Porphyria was excluded with the appropriate tests and the EEG and MRI did not show epileptogenic foci.

CT scan of the chest and abdomen and an MRI of the brain were unremarkable. Tests for tumour specific antigens were negative. Autopsy examination revealed a carcinoma arising from the right main bronchus spreading as a mass around the main bronchial wall and invading the adjacent lung. Histopathology confirmed its nature as small cell carcinoma and also showed typical neuropathological features of limbic encephalitis. This underlines the importance of considering paraneoplastic limbic encephalitis as an important differential diagnosis in an older patient with an acute or subacute onset of
dementia, impaired memory and psychiatric disturbances even in the absence of an overt malignancy. The measurement of antineuronal antibodies may help in diagnosing this condition.
Appendix 3:


37. Cunningham JD, Burt ME. Limbic encephalitis secondary to malignant thymoma.

38. Cher LM, Hochberg FH, et al. Therapy for paraneoplastic neurologic syndromes in
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39. Darnell RB, Posner JB. Paraneoplastic syndromes involving the nervous system.

40. Bak TH, Antoun N, Balan KK, Hodges JR. Memory lost, memory regained:
    neuropsychological findings and neuroimaging in two cases of paraneoplastic
    limbic encephalitis with radically different outcomes. Journal of Neurology,