Table 3 Diseases that can masquerade as ALS.

Anatomical abnormalities/compression syndromes
- Arnold-Chiari type I and other hindbrain malformations
- Cervical, foramen magnum or posterior fossa region tumours
- Cervical disc herniation with osteochondrosis
- Cervical meningioma
- Retropharyngeal tumour
- Spinal epidural cyst
- Spondylectic myelopathy and/or motor radiculopathy
- Syringomyelia

Acquired enzyme defects
- Adult GM1 gangliosidosis (hexosaminidase A or B deficiency)
- Polyglucosan body disease
- Pompe's Disease (Glycogen Storage Disease type II)

Autoimmune syndromes
- Mononuclear ganglioneuropathy with motor neuropathy
- Multifocal motor neuropathy with/without conduction block
- Dysimmune lower motor neuron syndromes (with GM1, GD1b, and asialo-GM1 antibodies)
- Other dysimmune lower motor neuron syndromes, including CIDP
- Multiple sclerosis
- Myasthenia gravis (in particular the anti-muscle-specific receptor tyrosine kinase positive variant)

Endocrine abnormalities
- Algodrome syndrome
- Diabetic 'amyotrophy'
- Insulinoma causing neuropathy
- Hypothyroidism with myopathy
- Hypothyroidism with myopathy
- Hyperparathyroidism (primary)
- Hyperparathyroidism (secondary due to vitamin D deficiency)
- Hypokalemia (Conn's syndrome)

Exogenous toxins
- Lead (?), mercury (?), cadmium, aluminium, arsenic, thallium, manganese, organic pesticides, neurotoxins, konzo

Infections
- Acute polioencephalitis
- Post-polioencephalitis progressive muscular atrophy syndrome
- HIV-1 (with vacular myelopathy)
- HTLV-1-associated myelopathy (tropical spastic paraplegia)
- Neuroborreliosis
- Syphilitic hyperreflexic pachymeningitis
- Spinal encephalitis lethargica, varicella-zoster
- Tichnosis
- Brucellosis, cat-scratch disease
- Prion disorders

Myopathies
- Cachectic myopathy
- Canceroid myopathy
- Dystrophin-deficient myopathy
- Inclusion body myositis
- Inflammatory myopathies
- Nemaline myopathy
- Polymyositis
- Sarcoïd myositis

Neoplastic syndromes
- Chronic lymphocytic leukaemia
- Intramedullary glioma
- Lymphoproliferative disorders with paraproteinaemia and/or oligodendral bands in the cerebrospinal fluid
- Pancoast tumour syndrome
- Paraneoplastic encephalomyelitis with anterior horn cell involvement

Table 3 (Continued)

- 'Still person plus' syndromes
- Physical injury
- Electric shock myoneuropathy
- Radiation-induced radiculoplexopathies and/myelopathy

Vascular disorders
- Arteriovenous malformation
- Dejerine's anterior bulbar artery syndrome
- Stroke
- Vasculitis

Other neurological conditions
- Western Pacific atypical forms of MND/ALS (Guam, New Guinea, Kii Peninsula of Japan)
- Caribbean atypical forms of MND—dementia—PSP (Guadeloupe)
- Madras-form of juvenile onset MND/ALS (South India)
- Frontotemporal dementia with MND/ALS (including Pick's disease with amyotrophy)
- Multiple system atrophy
- Olivopontocerebellar atrophy syndromes
- Primary lateral sclerosis (some subtypes not related to ALS)
- Progressive encephalomyelitis with rigidity
- PSP
- Hereditary spastic paraplegia (many variants, some subtypes with distal amyotrophy)
- Progressive spinal muscular atrophy (some subtypes not related to ALS)
- Spinobulbar muscular atrophy with/without dynactin or androgen receptor mutation
- Spinal muscular atrophy I-IV
- Brown-Vialetto—van Laere syndrome (early-onset bulbar and spinal ALS with sensorineural deafness)
- Fazio-Londe syndrome (infantile progressive bulbar palsy)
- Harper—Young syndrome (oblongatal and distal spinal muscular atrophy)
- Monomelic sporadic spinal muscular atrophy (benign focal myopathy, including Hirayama syndrome)
- Polynuropathies with dominating motor symptoms (like hereditary motor and sensory neuropathy type 2, hereditary motor neuropathy type 5)
- Familial amyloid polyneuropathy
- Benign fasciculations
- Myokymia

ALS, amyotrophic lateral sclerosis; MND, motor neuron disease; PSP, Progressive supranuclear palsy.

50% of the cases [16–19] (class IV). An evolution of atypical symptoms and a lack of progression of typical symptoms are the most important ‘red flags’ suggesting an alternative diagnosis [16]. The diagnosis should be regularly reviewed [18,19]. The revised El Escorial criteria [20, summarized in Table 4] are excessively restrictive and are not designed for use in routine clinical practice [21]. The new Awaji electrodiagnostic algorithm [22] added to the El Escorial criteria improves diagnostic sensitivity with no loss in specificity [23] and improves early diagnosis as shown in several class IV studies [24–27]. The clinician must decide, on the balance of probability, whether or not the patient has ALS, even in the absence of unequivocal