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LETTER TO THE EDITOR

Comorbid amyotrophic lateral sclerosis and sarcoidosis

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Dear Sir,

The comorbidity of amyotrophic lateral sclerosis (ALS) and sarcoidosis is rare. However, it might shed light on the role of inflammatory mechanisms in the development of motor neuron disease.

A 39-year-old right-handed man was admitted complaining of progressive slurred speech and swallowing difficulties. Examination revealed severe, diffuse atrophy, weakness and fasciculation of the tongue, and a slightly diminished gag reflex. Tendon reflexes were brisk in the upper and lower limbs bilaterally, and there were fasciculations in the deltoid and biceps muscles of the upper limbs, without obvious wasting or weakness other than mild left scapula winging. Sensory examination and coordination in the limbs were normal. An MRI of the brain with gadolinium (Fig. 1a, b), and an initial needle EMG of the muscles of the upper and lower limbs, did not reveal any pathological changes, but the patient's bulbar syndrome progressed. A repeat MRI of the brain with gadolinium was normal. CSF examination was normal. Routine laboratory tests were normal, including complete blood cell counts, routine biochemistry, erythrocyte sedimentation rate and C-reactive protein. Six months later needle EMG was repeated and it revealed frequent fasciculations of the chin and upper limb muscles. The patient was diagnosed with clinically probable laboratory-supported ALS by El Escorial criteria.

Two years earlier, he had developed a dry cough and shortness of breath after exertion. When his symptoms worsened in April 2021, he underwent a CT scan of the chest, which revealed enlarged mediastinal and pulmonary lymph nodes. Video-assisted thoracoscopic pulmonary lobectomy with subsequent histological analysis revealed the presence of non-caseating granulomas and giant cells confirming sarcoidosis (Fig. 1c). He was treated with tapering prednisolone starting at 30 mg daily, which improved his symptoms. He discontinued prednisolone in January 2022 at which time he experienced a transient improvement in his bulbar symptoms without recrudescence of his chest symptoms.

This patient with histopathologically confirmed sarcoidosis subsequently developed bulbar onset ALS. The normal MRI of the brain with gadolinium, CSF analysis, and typical EMG findings of ALS, allowed reasonable exclusion of neurosarcoidosis as the cause of his bulbar presentation. Neurosarcoidosis is an important differential diagnosis of bulbar ALS as it can manifest with meningeal infiltration at the base of skull causing multiple cranial neuropathies, or manifest with parenchymal lesions in the brainstem leading to bulbar or pseudobulbar palsies [1–3].

Amyotrophic lateral sclerosis and sarcoidosis occurring comorbidly are not common. However, according to a retrospective analysis by Streicher et al. [4], it occurs more frequently than should be expected by chance. The estimated likelihood of the coincidence of the two conditions should be no more than 1 case per 1000 patients with ALS, but a retrospective analysis from the US revealed 6 per 1000 patients in an ALS cohort. To date, there have been eleven case reports of ALS and sarcoidosis occurring comorbidly, including one retrospective case series of six patients [1–6].

Eight of the eleven patients with both ALS and sarcoidosis were females, and nine of the eleven had a spinal onset of the disease. Sarcoidosis was diagnosed simultaneously with ALS onset in three out of five cases. In one case, granulomatous disease was detected in lymph nodes at autopsy, and in another case it was diagnosed histopathologically one month prior to ALS onset. The authors reported the results of the treatment of sarcoidosis in four out of five cases, which included corticosteroids, cytostatic medications, plasmapheresis and infliximab. None of these treatments changed the progressive course of their ALS [1–6].

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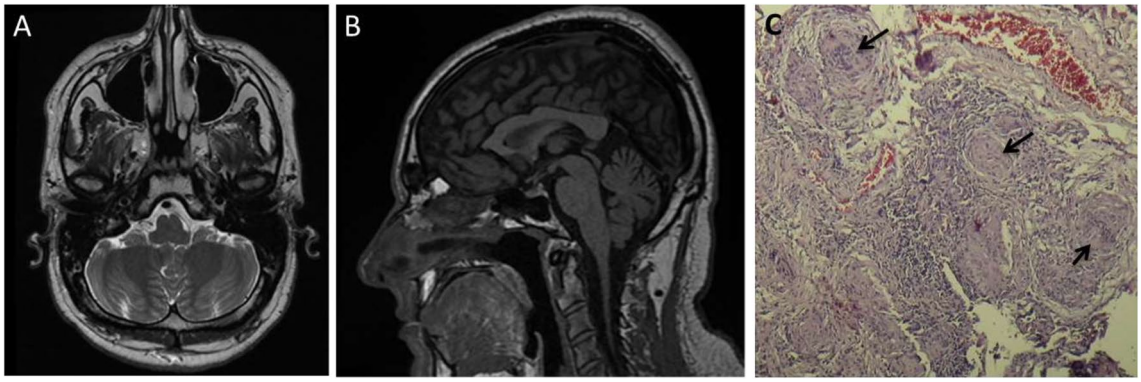

Fig. 1 Representative axial T2 weighted image from the patient's MRI of the brain showing a normal brainstem (**A**). Representative axial T1 weighted post-gadolinium image from the patient's MRI of the brain showing no evidence of leptomeningeal enhancement (**B**). Non-caseating granulomas (arrows) in the biopsied mediastinal lymph node consistent with sarcoidosis (hematoxylin–eosin staining, X100) (**C**)

ALS is a typical neurodegenerative disease, however, immunopathogenetic mechanisms, involving alterations of T-cells, monocytes, complement and cytokines, play a substantial role in its development [5]. While sarcoidosis and ALS in these patients may be unrelated conditions, it is possible that sarcoidosis could be a trigger of ALS in some patients by initiating an inflammatory response in the central nervous system such as infiltration of immune cells, activation of microglia and astrocytes or via the breakdown of blood–brain and blood–spinal cord barrier. On the other hand, sarcoidosis is characterized by immunodeficiency [1–3] which could also suppress the neuroprotective effects of the immune system in the early stages of ALS. In theory, ALS could trigger sarcoidosis by similar mechanisms, but our case would seem to contradict this hypothesis, as the clinical manifestations of sarcoidosis predated ALS onset. Lastly, the same unidentified factors could trigger both diseases, although presumably the co-existence of the diseases would be more common if that was the case. More detailed investigation of the patients with coincident ALS and sarcoidosis, including immunogenetic profiling, may shed light on the plausibility of immunological triggers for ALS in these patients.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from the patient included in the case report.

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