Amyotrophic lateral sclerosis with brain white matter lesion in a young patient carrying FUS R521C mutation: case report

E. Distaso, E. D'Errico, L. Conforti*, A. Scarafino, R. Cortese, I. Tempesta, A. Mastronardi and I. L. Simone

Department of Basic Medical Sciences, Neurosciences and Sense Organs - University "A. Moro" of Bari - Bari, Italy
*** Institute of Neurological Sciences - National Research Council, Mangone - Cosenza**

Background*:* Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease involving upper and lower motorneuron. Genetic mutations are detected in a minority of patients, and specific genes are involved. Even if ALS is not a white matter pathology, in some rare cases it has been described the coexistence of brain white matter lesions (WMLs). We present the case of a sporadic ALS patient carrying a FUS/TLS mutation and showing brain white matter lesions (WMLs).

Case Description: A young 36 years old woman came to our attention complaining of a rapidly progressive history of upper limbs weakness from five months, successively involving lower limbs with recurrent stumbling, and dyspnea. Clinical and familial history was unremarkable. Previous brain MRI investigation showed multiple T2 and FLAIR (Fig.1 and 2) hyperintense periventricular and subcortical WMLs, without gadolinium enhancement. Spinal cord was normal. Previous electromyography revealed chronic neurogenic damage with motor unit loss, suggestive of motoneuron disease. Neurological examination at admission was characterized by spastic paresis in lower limbs and flaccid paralysis in upper limbs with diffuse muscular atrophy. Deep tendon reflexes were brisk in lower limbs and reduced in the upper limbs. Diffuse fasciculations were detected. Routine blood tests were all normal, except for a high title of AntiTPO antibodies associated with a mild increase in TSH blood levels. Cerebrospinal fluid analysis showed only a mild blood-brain barrier damage, without cell increase or oligoclonal bands. A new brain and spinal cord MRI confirmed the presence of periventricular and subcortical WMLs, without gadolinium enhancement. At electromyography a marked and diffuse denervation with fasciculations and fibrillations in four limbs was detected. Muscle biopsy revealed neurogenic atrophy. Genetic test showed a pR521C mutation in exon 15 of the FUS/TLS gene. Patient rapidly worsened showing severe progressive dysphagia, tetraplegia and hypoventilation. Death came after 14 months from symptoms onset for respiratory failure.

Fig. 1 FLAIR MRI IMMAGES

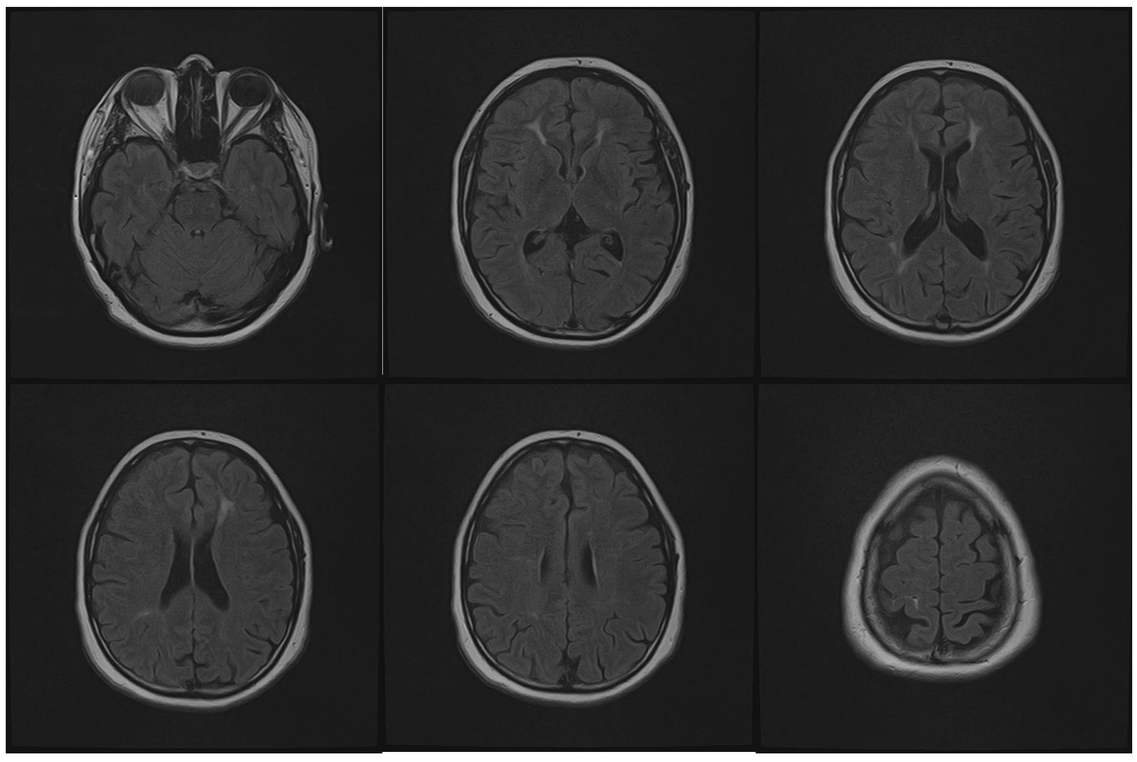
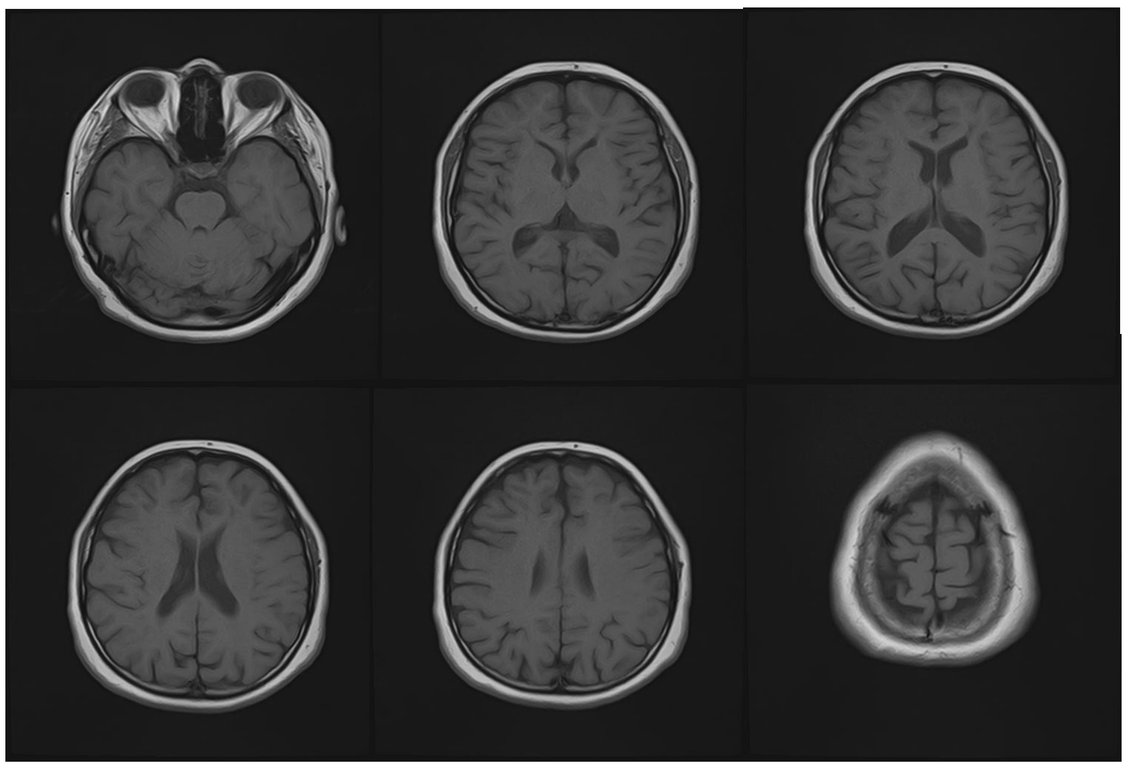


Fig. 2 T1 WEIGHTED MRI IMMAGES



Conclusions: To our best knowledge, this is the first described patient with ALS carrying FUS/TLS pR521C mutation associated with brain white matter lesions and a rapidly fatal outcome. This association might be accidental or on the other hand suggestive of a process of demyelination and or gliosis associated with the mutation of FUS/TLS.

References:

- Andreadou E1, Sgouropoulos P, Varelas P, Gouliamos A, Papageorgiou C. Subcortical frontal lesions on MRI in patients with motor neurone disease. Neuroradiology. 1998 May;40(5):298-302.
- Ticozzi N, Tiloca C, Mencacci NE, Morelli C, Doretti A, Rusconi D, Colombrita C, Sangalli D, Verde F, Finelli P, Messina S, Ratti A, Silani V. Oligoclonal bands in the cerebrospinal fluid of amyotrophic lateral sclerosis patients with disease-associated mutations. J Neurol. 2013 Jan;260(1):85-92. doi: 10.1007/s00415-012-6589-0
- Sproviero W, La Bella V, Mazzei R, Valentino P, Rodolico C, Simone IL, Logroscino G, Ungaro C, Magariello A, Patitucci A, Tedeschi G, Spataro R, Condino F, Bono F, Citrigno L, Monsurrù MR, Muglia M, Gambardella A, Quattrone A, Conforti FL. FUS mutations in sporadic amyotrophic lateral sclerosis: clinical and genetic analysis. Neurobiol Aging. 2012 Apr;33(4):837.e1-5. doi: 10.1016/j.neurobiolaging.2011.10.005

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