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Until All Primary and Secondary Causes of Sensory Neuropathy Were Ruled Out, Sensory Deficits Should Not Be Considered Inherent in ALS

Josef Finsterer

MD, PhD, Neurology Dpt., Neurology & Neurophysiology Center, Vienna, Austria, Orcid: 0000-0003-2839-7305

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LETTER TO THE EDITOR

We were interested to read the article by Santos, *et al*. on a case series of three patients with sporadic amyotrophic lateral sclerosis (sALS) who also developed sensory disturbances [Oliveira Santos, M. *et al*., 2025]. The sensory disturbances occurred before or overlapped with the motor symptoms in the same region and followed the same pattern of lower motor neuron involvement over the course of the disease [Oliveira Santos, M. *et al*., 2025]. Two patients also had bilateral involvement of the trigeminal sensory fibers [Oliveira Santos, M. *et al*., 2025]. It was concluded that motor neuron disease should be considered as a neurodegenerative multisystem disease and that sensory neuropathy, although very rare, should not be neglected as a possible part of the disease spectrum [Oliveira Santos, M. *et al*., 2025]. The study is noteworthy, but some points should be discussed.

The first point is that familial ALS (fALS) has not been sufficiently ruled out [Oliveira Santos, M. *et al*., 2025]. Several cases with fALS have been reported that showed not only motor symptoms but also sensory deficits. Sensory dysfunction was reported in a 67-year-old woman with fALS due to a variant in the *MFN2* gene [Vinciguerra, C. *et al*., 2023]. fALS with sensory dysfunction was also described in a Japanese patient with fALS due to a *SOD1* variant [Sakamoto, H. *et al*., 2014]. The absence of a positive family history of fALS does not rule out fALS, as the causative mutation may have occurred sporadically. There is also evidence from animal studies that the sensory system may be affected in fALS [Kuźma-Kozakiewicz, M. *et al*., 2013]. Patient-1 was tested for *C9orf72* and was negative. He carried a variant of unknown significance in *hnRNPA2B1* [Oliveira Santos, M. *et al*., 2025]. Patient-2 tested negative for mutations in *C9orf72*, *SOD1* and *TARDBP*. Patient-3 was tested for *C9orf72* and a panel without specifying the genes tested and was negative [Oliveira Santos, M. *et al*., 2025]. However, more than 40 genes are currently known to be associated with fALS [Ghasemi, M. *et al*., 2018].

The second point is that a second disorder in addition to sALS has not been sufficiently excluded. The most important second disorder explaining the clinical picture would be hereditary sensory and autonomic neuropathy (HSAN). To rule out HSAN, a panel test for mutated genes associated with hereditary neuropathy or a WES would need to be performed. We should also know if sporadic bulbospinal muscular atrophy with facial sensory neuropathy has been ruled out [Isoardo, G. *et al*., 2008]. Another differential diagnosis that mimics ALS and may have sensory disturbances is mitochondrial disorder (MID) [Finsterer, J, 2002]. Several patients with MID and upper and lower motor neuron involvement and sensory disturbances have been reported [Finsterer, J, 2002]. In addition, have all secondary causes of sensory neuropathy (metabolic, endocrine, toxic, vascular, immunologic, paraneoplastic, neoplastic) been carefully excluded?

The third point is that patient-1 received chemotherapy two years before the ALS diagnosis [Oliveira Santos, M. *et al*., 2025]. Is it conceivable that the sensory neuropathy was toxic due to the chemotherapy? Did patient-1 receive long-term hormone therapy?

The fourth point is that different diagnostic criteria were applied [Oliveira Santos, M. *et al*., 2025]. Patient-1 and Patient-2 were diagnosed according to the revised El Escorial criteria and the Awaji-Shima criteria, while Patient-3 was diagnosed according to the Gold Coast criteria [Oliveira Santos, M. *et al*., 2025]. Did patient-1 and patient-2 also fulfil the Gold Coast criteria?

***Corresponding Author:** Josef Finsterer

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To summarize, this interesting study has limitations that affect the results and their interpretation. Addressing these limitations could strengthen the conclusions and support the message of the study. Until all primary and secondary causes of sensory neuropathy have been thoroughly ruled out, sensory deficits in ALS should not be categorized as part of the clinical presentation.

REFERENCES

1. Oliveira Santos, M., Pinto, S., Silveira, F., Gromicho, M., Alves, I., Castro, J., Castro, I. & de Carvalho, M. "Amyotrophic lateral sclerosis associated with severe sensory neuronopathy: Case series." *Journal of Clinical Neuromuscular Disease*, 26.3 (2025): 133–139.
2. Vinciguerra, C., Di Fonzo, A., Monfrini, E., Ronchi, D., Cuoco, S., Piscosquito, G., Barone, P. & Pellecchia, M. T. "Case report: Asp194Ala variant in MFN2 is associated with ALS-FTD in an Italian family." *Frontiers in Genetics*, 14 (2023): 1235887.
3. Sakamoto, H., Akamatsu, M., Hirano, M., Saigoh, K., Ueno, S., Isono, C., Kusunoki, S. & Nakamura, Y. "Multiple system involvement in a Japanese patient with a V31A mutation in the SOD1 gene." *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 15.3–4 (2014): 312–314.
4. Kuźma-Kozakiewicz, M., Chudy, A., Gajewska, B., Dziewulska, D., Usarek, E. & Barańczyk-Kuźma, A. "Kinesin expression in the central nervous system of humans and transgenic hSOD1G93A mice with amyotrophic lateral sclerosis." *Neurodegenerative Diseases*, 12.2 (2013): 71–80.
5. Guo, Y. S., Wu, D. X., Wu, H. R., Wu, S. Y., Yang, C., Li, B., Bu, H., Zhang, Y. S. & Li, C. Y. "Sensory involvement in the SOD1-G93A mouse model of amyotrophic lateral sclerosis." *Experimental & Molecular Medicine*, 41.3 (2009): 140–150.
6. Ghasemi, M. & Brown, R. H. Jr. "Genetics of amyotrophic lateral sclerosis." *Cold Spring Harbor Perspectives in Medicine*, 8.5 (2018): a024125.
7. Isoardo, G. & Troni, W. "Sporadic bulbospinal muscle atrophy with facial-onset sensory neuropathy." *Muscle & Nerve*, 37.5 (2008): 659–662.
8. Finsterer, J. "Mitochondriopathy as a differential diagnosis of amyotrophic lateral sclerosis." *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders*, 3.4 (2002): 219–224.

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