PRNP P102L MUTATION AND VALINE AT CODON 129 ASSOCIATED WITH PROGRESSIVE MYOCLONUS EPILEPSY: A CASE REPORT

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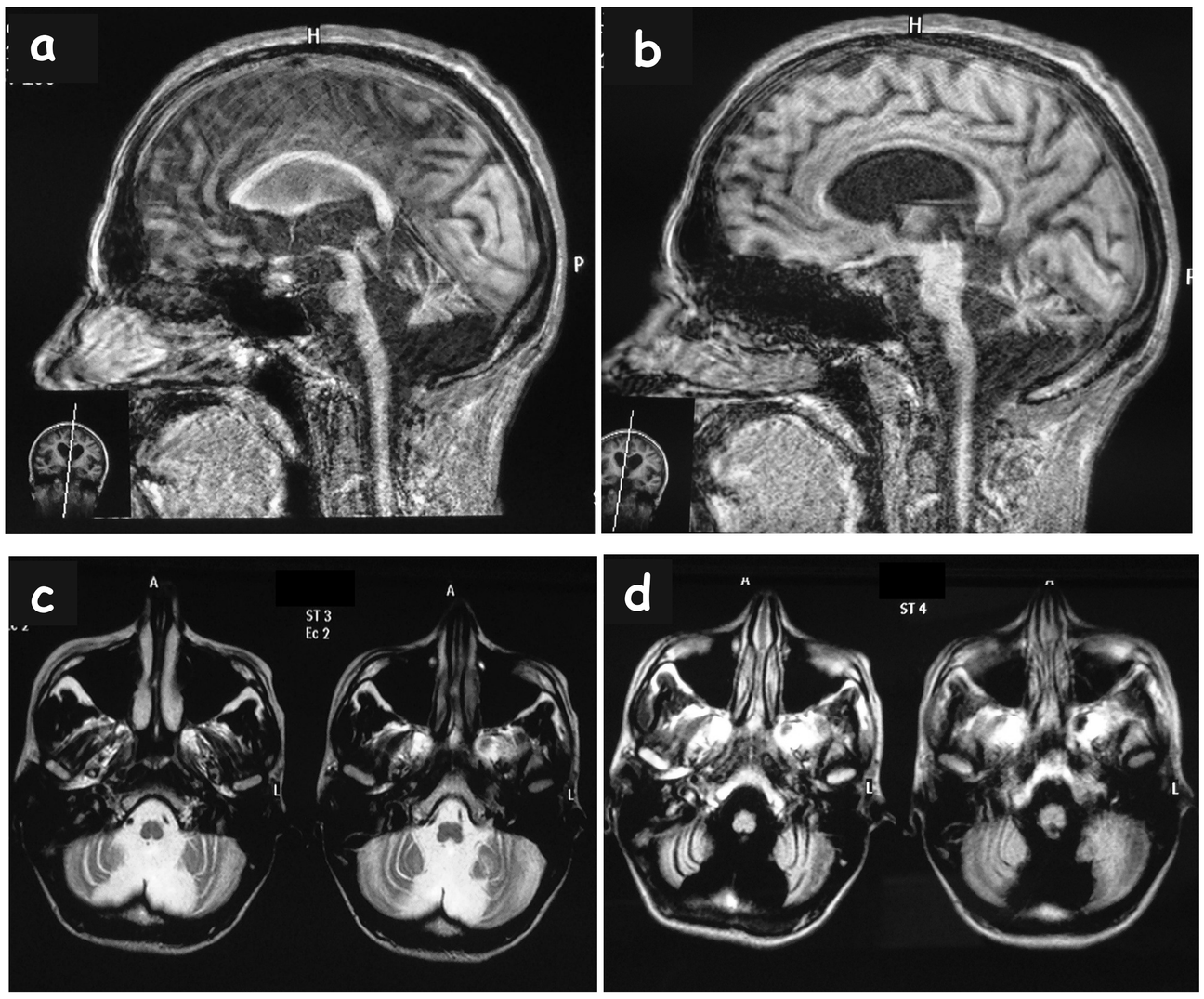
OBJECTIVE

Progressive Myoclonus Epilepsies (PMEs) are a group of rare diseases characterized by myoclonic or tonic-clonic seizures and progressive neurological deterioration, typically with cerebellar signs and dementia that vary across different PMEs. Here, we report the clinical feature of a patient with PME phenotype in whom whole exome sequencing (WES) revealed the PRNP P102L mutation and valine at codon 129.

CASE REPORT

From the age of 25 years, a 38-year-old woman developed unsteadiness, slow movements and difficulty to speak. Four years later, spontaneous and reflex myoclonus appeared, involving both arms, while cognitive decline started when she was 32-year-old. She also developed generalized clonic-tonic-clonic seizures that were controlled by valproate. All other symptoms worsened over the time and, at the age 37, she became bedridden and mutacic with spastic tetraparesis. She died at the age 38 as consequence of refractory convulsive status epilepticus. Brain MRI showed marked atrophy in cerebellar vermis, EEG-EMG polygraphic study showed spontaneous, reflex and action myoclonus associated with generalized sharp-waves and photo-paroxysmal response. Her father deceased at the age 45 of the same disease. The common genetic testing for PMEs was negative. WES revealed an heterozygous mutation in the PRNP gene encoding for prion protein, characterized by the replacement of proline with leucine at codon 102 (p.P102L). The polymorphism 129 Met/Val was also identified.



Paramedian (b) and median (a) sagittal T1-weighted images sections show marked brainstem and cerebellar atrophy. Axial T2-weighted images (d) and axial FLAIR section (c) show cerebellar atrophy more evident in vermis.

CONCLUSIONS

Identification of a heterozygous mutation encoding p.Pro102Leu in this patient with PME was an unexpected finding. This previously described pathogenic mutation in PRNP is a recurrent cause of the Gerstmann-Straussler-Scheinker (GSS) disease. Notably, the mutation in our patient occurred in the same allele with p.Met129Val, a common polymorphism and a known modulator of prion diseases. Having these two variants in the same allele leads to a remarkably different disease presentation than with p.Pro102Leu alone and the reported cases have also had seizures. Thus, we believe that the diagnosis of GSS should be considered in addition to other causes in patients with PME.

REFERENCES

1 Shahwan A, Farrell M, Delanty N. Progressive myoclonus epilepsies: a review of genetic and therapeutic aspects. Lancet Neurol 2005;4:239-48.

2 Bianca, M. *et al.* Gerstmann–Sträussler–Scheinker disease with P102L–V129 mutation: a case with psychiatric manifestations at onset. *Ann. Genet.* 2003; 46: 467-9.

3 Young, K., Clark, H.B., Piccardo, P., Dlouhy, S.R. & Ghetti, B. Gerstmann–Sträussler–Scheinker disease with the PRNP P102L mutation and valine at codon 129. *Brain Res. Mol. Brain Res. 1997;* 44: 147-50.

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