Fondazione IRCCS Ca' Granda
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Evidence of CNS beta-amyloid deposition in Nasu-Hakola disease due to the *TREM2* Q33X mutation

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Backgroung

Nasu-Hakola disease (NHD), also known as polycystic lipomembranous osteodysplasia and sclerosing leukoencephalopathy (PLOSL), is a rare **autosomal recessive disorder** characterized by multifocal bone cysts and early onset dementia, caused by a loss-of-function mutation of either *DAP12* or *TREM2* (Triggering Receptor Expressed on Myeloid cells) genes, involved in surface signalling in myeloid cells

Case report

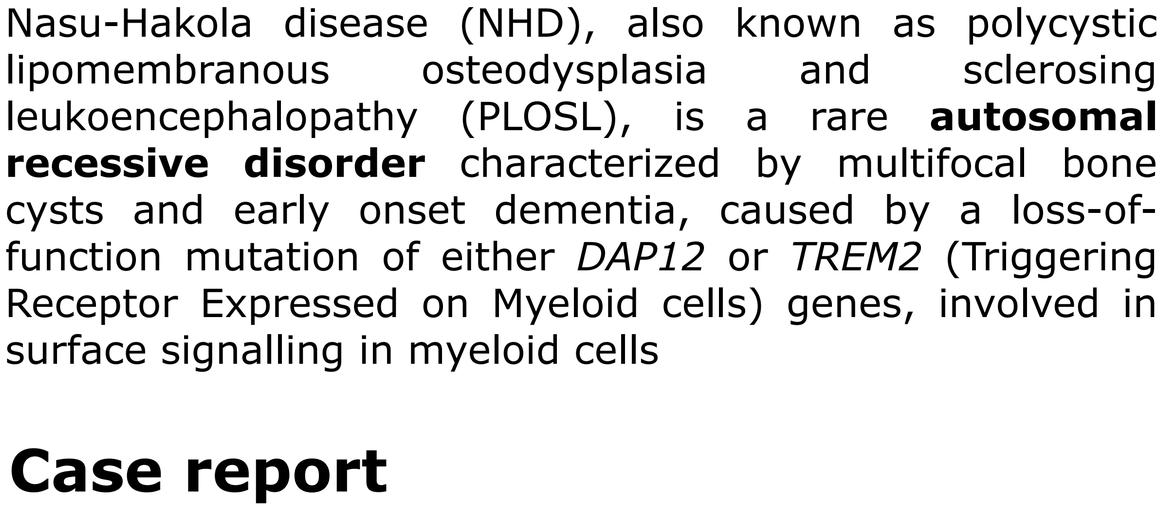
A 39 years old woman was referred to our Neurology Department complaining of a **two-years history of progressive cognitive impairment**, with memory disturbances and disorientation in time and place, associated with personality changes; occasional atonic-tonic seizures have also been reported.
Family history was unremarkable.

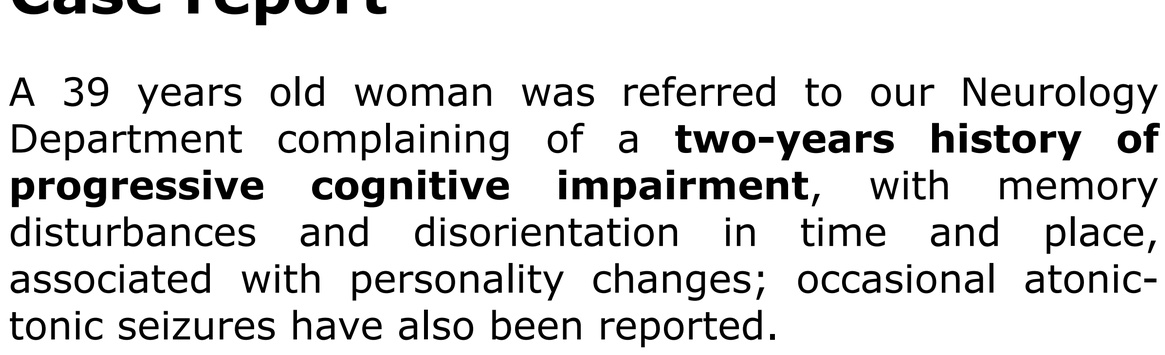
Neuropsychological evaluation outlined a moderate cognitive impairment, involving all cognitive functions examined, except for the working memory domain
Brain MRI showed widespread cortical atrophy and diffuse white matter hyperintensity in T2W sequences **(Fig. A)**, with glucose temporoparietal hypometabolism on FDG PET scan **(Fig. B)**.

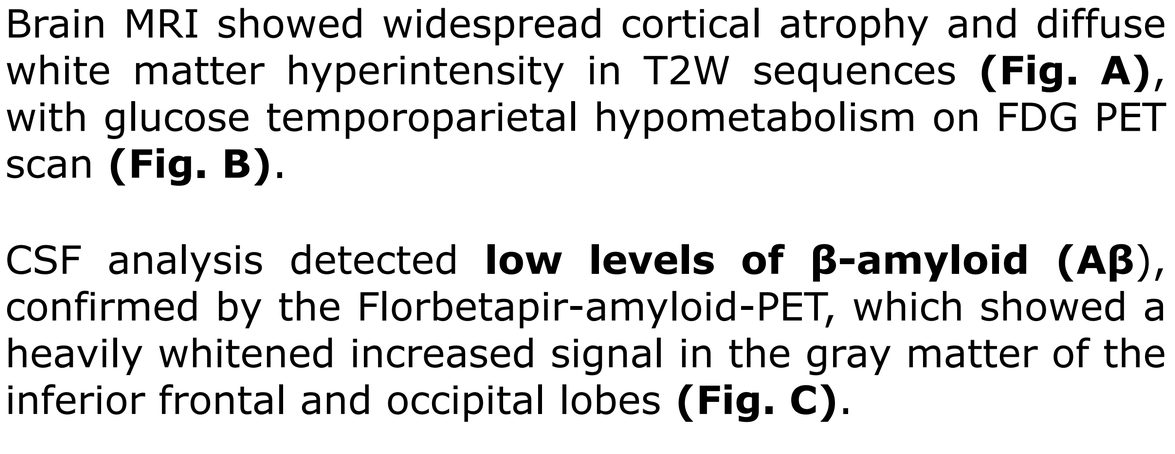
CSF analysis detected **low levels of β-amyloid (Aβ**), confirmed by the Florbetapir-amyloid-PET, which showed a heavily whitened increased signal in the gray matter of the inferior frontal and occipital lobes **(Fig. C)**.

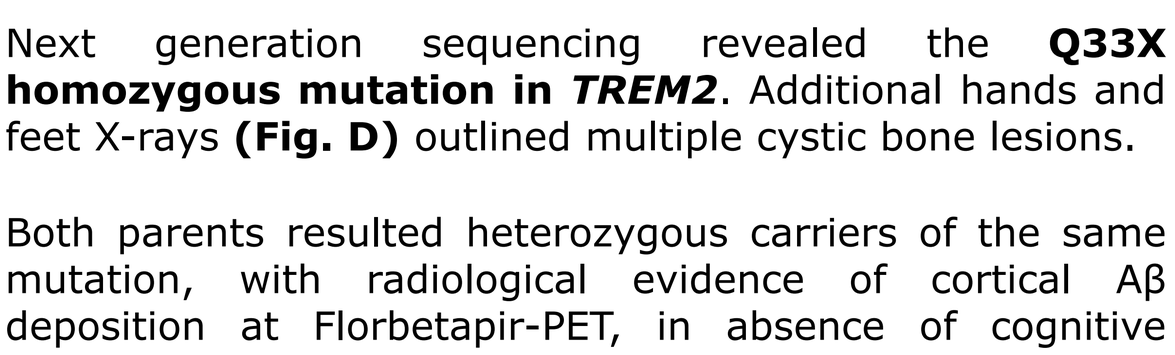
Next generation sequencing revealed the **Q33X homozygous mutation in *TREM2***. Additional hands and feet X-rays **(Fig. D)** outlined multiple cystic bone lesions.

Both parents resulted heterozygous carriers of the same mutation, with radiological evidence of cortical Aβ deposition at Florbetapir-PET, in absence of cognitive impairment.









Conclusion

Aβ deposition in the CNS occurs in NHD; this finding suggests the existence of common mechanisms between NHD and AD pathogenesis and the potential involvement of microglia in both formation and clearance of Aβ.

References

Paloneva J, Autti T, Raininko R, Partanen J, Salonen O, Puranen M, Hakola P, Haltia M: CNS manifestations of Nasu-Hakola disease: a frontal dementia with bone cysts. Neurology 2001; 56: 1552–1558;
Yaghmoor F, Noorsaeed A, Alsaggaf S, Aljohani W, Scholtzova H, Boutajangout A, et al. The Role of TREM2 in Alzheimer's Disease and Other Neurological Disorders. J Alzheimers Dis Parkinsonism. 2014 Nov;

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