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Excess mortality, causes of death and last EDSS score prior to death in patients with AQP4 antibody positive neuromyelitis optica spectrum disorder

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Introduction:

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune disease of the central nervous system that often causes severe disability due to relapses. Long-term treatment, including immunosuppressive therapy (IST), is recommended to prevent relapses but may increase the risk of infection and malignancy.

Objectives/Aims:

To determine excess mortality in patients with aquaporin-4 antibody positive (AQP4+) NMOSD, describe causes of death, and characterise last Expanded Disability Status Scale (EDSS) score prior to death.

Methods:

This retrospective study reviewed records of patients with AQP4+ NMOSD in the UK cohort from 2014 to either 2020 or death. Cause of death could be attributed to NMOSD-related disability and/or end stage infection, relapse, immunosuppression, coexisting autoimmune disease, or unlikely related to NMOSD.

Standardised mortality ratio (SMR) was calculated by dividing the observed mortality rate in the NMOSD cohort by that of the UK population, adjusting for age, sex, and race. Excess mortality was calculated by subtracting adjusted UK mortality from observed NMOSD mortality.

Linear regression assessed the relationship between last EDSS score prior to death and disease duration.

Results:

Of 158 AQP4+ patients in the NMOSD cohort, 22 died. 7 deaths were from complications related to severe disability and 1 from brainstem relapse. None died of associated autoimmune disease; 1 died of malignancy that may have resulted from immunosuppression. 12 deaths were considered unlikely related to NMOSD; cause of death was undetermined for 1.

Median age at death was 66 years (range 16-88); median last EDSS prior to death was 7.0 (range 3.0-9.0). Mean annual death rate in the NMOSD cohort was 2.64% compared with 0.68% in the matched population. SMR was 3.88 (95% CI 1.23-7.33) with an excess mortality of 1.96% per year in the NMOSD cohort.

Last EDSS score prior to death was not significantly associated with disease duration (p=0.88).

Conclusion:

Compared to the general population, patients with AQP4+ NMOSD are at ~4 times greater risk of death, although their deaths may have been more systematically documented. While only 1 death was possibly immunosuppression-related, 8 (36.3%) were disability or relapse associated. Further, data on last EDSS score prior to death suggest mortality in NMOSD is unpredictable. These findings may justify long-term use of therapies to prevent relapse and disability in NMOSD.

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