Prevalence of Iatrogenic Central Nervous System Inflammation at a Tertiary Neuroimmunology Clinic

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BACKGROUND

- Increased utilization of biologic therapies—including tumor-necrosis-factor-alpha inhibitors (TNFAIs) for autoimmune diseases and immune-checkpoint inhibitors (ICIs) for cancer—has coincided with a rise in CNS inflammatory adverse events[1,2]
- The recent mass vaccination against SARS-CoV-2 has renewed scientific interest in iatrogenic immune-mediated reactions
- The prevalence of iatrogenic events in the neuroimmunology clinic is unknown

OBJECTIVE

- To evaluate the prevalence and clinical characteristics of iatrogenic CNS inflammation at a tertiary neuroimmunology clinic

METHODS

- Adult patients seen over 5 years (1/2017-12/2021) at a tertiary neuroimmunology clinic were screened for exposure to vaccines, TNFAIS, and ICIs
- In patients with suspected iatrogenic events, the Naranjo Adverse Drug Reaction Probability Scale was used to score the probability of iatrogenicity[3]
- Differences in disease phenotypes and courses, responses to treatment, and patient characteristics were studied in relation to TNFAI, ICI, and vaccine exposure
- These clinical characteristics were compared between patients with autoimmune diseases with and without exposure to TNFAIs and in cancer patients with and without exposure to ICIs

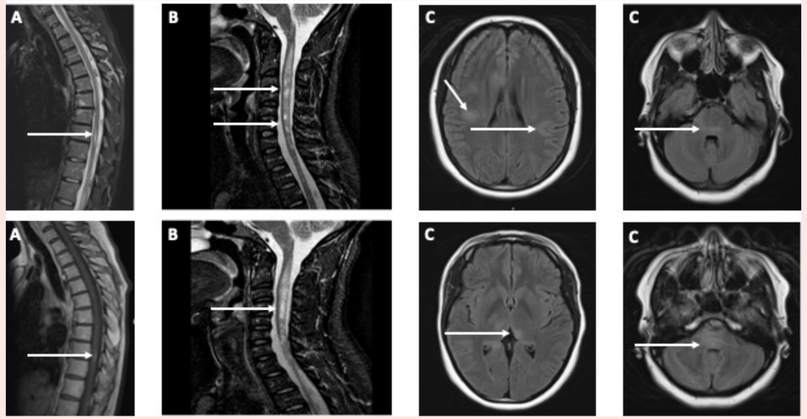

Figure 1: Brain and spinal cord MRI images showing vaccine-related iatrogenic CNS inflammatory events.
(A) A case of probable post-mRNA COVID-19 vaccine-induced short segment thoracic myelitis; **(B)** A case of post-influenza vaccine NMOSD with AQP4-IgG attack; **(C)** A case of probable anti-MOG multifocal demyelination and brainstem encephalitis following MMR, tetanus, and VZV vaccinations
Arrows point to the abnormal signals in the brain and spinal cord.

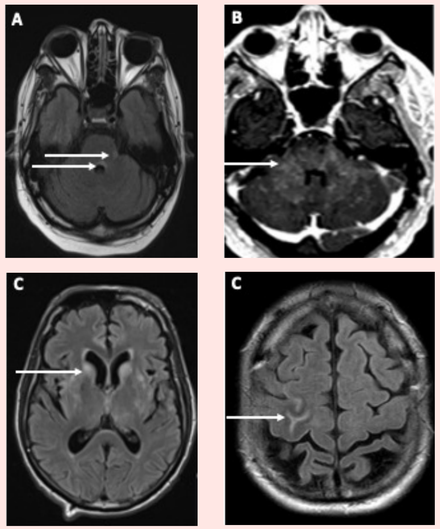

Figure 2: Brain MRI images showing TNFAI-related iatrogenic CNS inflammatory events.

(A) A case of probable etanercept-related MS relapse
(B) A case of probable adalimumab-related NMDAR-IgG encephalitis overlapping with CLIPPERS syndrome
(C) A case of probable adalimumab-related autoimmune encephalitis.
Arrows point to the abnormal signals in the brain.

Figure 3: Brain and spinal cord MRI images showing ICI-related iatrogenic CNS inflammatory events.
(A) A case of probable nivolumab/ipilimumab–induced transverse myelitis; **(B)** A case of probable nivolumab-induced double seronegative NMOSD.
Arrows point to the abnormal signals in the brain and spinal cord.

RESULTS

- 422 adult patients were analyzed and 27 potential iatrogenic events were observed, accounting for 6.4% of new referrals
- 74% of potential iatrogenic events scored as probable and 26% as possible
- Clinical phenotypes included MS relapses (37%); autoimmune encephalitis (30%); NMOSD attacks (15%); transverse myelitis (11%); optic neuritis (4%); and MOGAD attacks (4%)
- A monophasic course was observed in 44% of cases while 41% were relapsing
- 41% were fully-responsive to corticosteroids

RESULTS

- More probable events were observed in the ICI and vaccine groups compared to more possible events in the TNFAI group
- Both the vaccine and ICI groups had higher Naranjo scores than the TNFAI group
- The ICI group was more likely to present with monophasic autoimmune encephalitis
- The TNFAI group had a longer interval from exposure to the potential iatrogenic event compared to the vaccine and ICI groups
- No significant differences were observed between patients with autoimmune diseases with and without exposure to TNFAIs in terms of baseline demographics, neurological disease course or phenotype, and response to immunotherapies
- Cancer patients exposed to ICIs were more likely to have a monophasic neurological disorder and present with autoimmune encephalitis than cancer patients not exposed to ICIs

CONCLUSIONS

- Iatrogenic CNS inflammation is rare and typically involves steroid-responsive monophasic events
- A subset of iatrogenic events can unmask or worsen relapsing disorders
- Iatrogenicity was more probable with vaccines and ICIs compared to TNFAIs

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