Anti-GABA$_A$ receptor encephalitis 14 months after allogeneic haematopoietic stem-cell transplant for acute myeloid leukaemia

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A 61-year-old man was admitted to our hospital with a 5-day history of sudden-onset, persistent myocloni in his left leg and the left side of his abdomen. Previously, the patient had been fit and well. He reported no recent fever, headache, or trauma.

14 months before admission, the patient had an allogeneic haematopoietic stem cell transplantation for acute myeloid leukaemia with mutated *nucleophosmin 1* which resulted in full remission.

On examination, we found the patient generally well; he had painless, rhythmic myocloni, with a frequency of 0·5–1·0 per s, of the proximal left leg and abdomen. The movements were continuous and would not be triggered or suppressed by any specific movements. The patient had no other atypical findings and cognitively was fully alert and conscious.

Laboratory investigations—apart from a previously described macrocytosis—were within typical range.

On day 1 after admission, an MRI of the patient's brain showed multiple cortico-subcortical fluid-attenuated-inversion-recovery hyperintense lesions without diffusion restrictions or contrast-enhancement (figure).

On day 2 after admission, cerebrospinal fluid (CSF) analyses showed normal cell and protein count; microbial multiplex PCR testing and cytology tests for malignancies were negative.

On day 3, a scalp electroencephalogram (EEG) showed no epileptiform discharges that correlated with the myocloni. Further investigations found no neoplasms.

On day 5, the myocloni extended to the proximal part of the left arm despite the patient being given multiple antiseizure medications.

On day 8 after admission, a biopsy of the brain was done and histopathological analysis of a sample of the biopsy showed T-cell-dominated perivascular lymphocyte infiltrates and endothelial proliferations without evidence of viral infection, demyelination, graft-versus-host disease, or neoplasia.

From day 9 after admission, the patient's condition deteriorated; he became disorientated and confused, then drowsy and stuporous; the myocloni continued.

Repeated MRIs, from days 5 to 12 after admission, showed progression of the multiple cortico-subcortical lesions (figure); the EEG showed right-hemispheric temporo-parietal focal slowing independent of the worsening of the patient's condition.

On day 15 after admission, he developed electroclinical super-refractory status epilepticus, which was finally terminated by continuous intravenous thiopental. At this stage autoimmune encephalitis was suspected and immunosuppressive treatment with prednisolone, plasmapheresis, intravenous immunoglobulins, and rituximab started; serum and CSF—collected prior to initiation of the treatments—was subsequently found to be positive for GABA$_A$ receptor antibodies (serum titre 1:320; normal <1:20; CSF titre 1:1), confirming the diagnosis of anti-GABA$_A$ receptor encephalitis.

On day 33 and day 185, MRIs showed improvement (figure) with concomitant decreases in serum antibody titres (day 79, 1:20; day 186, <1:20) and serum neurofilament light chain concentrations—day 34, 511·5 pg/mL (99·995 percentile); day 233, 25·4 pg/mL (97·20 percentile).

During the period of hospitalisation, the patient experienced multiple complications, including asystole, which required resuscitation, and critical-illness polyneuromyopathy. After a prolonged stay in the intensive care unit, the patient was transferred to a neurorehabilitation unit.

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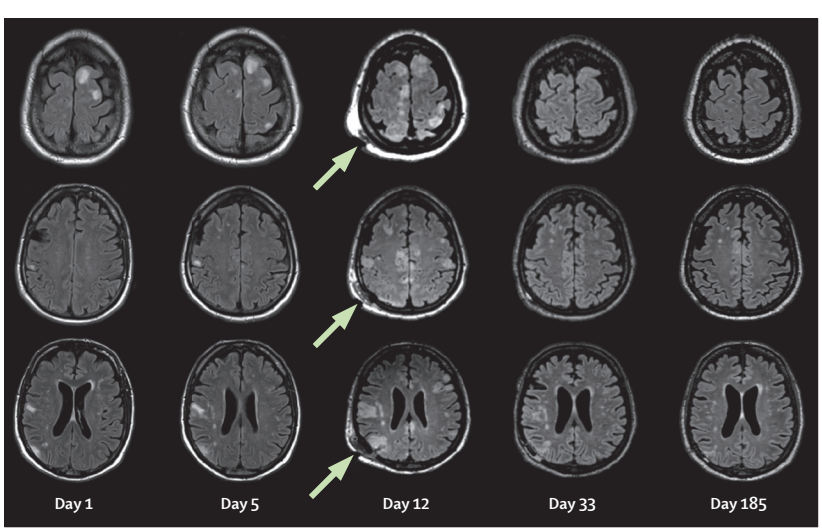

Figure: **Anti-GABA$_A$ receptor encephalitis 14 months after allogeneic haematopoietic stem-cell transplant for acute myeloid leukaemia**

Serial axial fluid-attenuated-inversion-recovery MRIs done on the day of admission (day 1), day 5, day 12, day 33, and at follow-up on day 185, showing supratentorial, bi-hemispheric, multifocal, non-confluent cortico-subcortical hyperintense lesions without diffusion restriction or contrast-enhancement (not shown). Notably, lesion progression decreased after treatment initiation on day 15. The focal tissue swelling in the right parietal region on day 12 is attributed to a brain biopsy (arrows).

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See **Online** for video

At outpatient follow-up, the patient was ambulatory and had mild, residual paresis of his left leg (video); his neurological deficits continued to improve.

Autoantibodies against $GABA_A$ receptor cause an encephalitis characterised by seizures, cognitive impairment, psychiatric symptoms, and movement disorders. Underlying pathogenic mechanisms are, in most cases, unclear; associations between haematological malignancies and allogeneic haematopoietic stem cell transplants—as in our case—causing immune dysregulation may indicate possible aetiologies. Studies have reported a range of 9 to 43 months from completion of allogeneic haematopoietic stem cell transplant to the development of $GABA_A$ receptor encephalitis.

Typical MRI changes, in conjunction with the patient's history and symptoms, should prompt consideration of anti-$GABA_A$ receptor encephalitis; confirmatory autoantibody results—often available only after a significant length of time—should not delay treatment initiation.

Contributors

We all provided care for the patient, and revised the manuscript. TR, ÖY, and UFisch collected data and wrote the first draft of the manuscript. Written consent for publication was obtained from the patient.

Declaration of interests

We declare no competing interests relating to the content of the manuscript. ÖY reports honoraria from Biogen. HHH reports grants from Moderna to the University of Basel; and he reports personal consulting fees from AlCuris, Allovir, Moderna, VeraTX, and Roche, and personal honoraria from VeraTX, Takeda, Biotest, and Gilead. UFischer reports research grants from the Swiss National Science Foundation, the Swiss Heart Foundation, Medtronic, Stryker, Penumbra, Rapid medical, Phenox, and Boehringer Ingelheim; consulting fees from Medtronic, Stryker, CSL Behring (fees paid to institution); has membership in a data safety monitoring board for the TITAN trial, IN EXTREMIS trial, LATE-MT trial, Rapid Puls Trial; has membership in the Clinical Event Committee of the COATING Trial (Phenox) and membership in the advisory board for CLS Behring, Acthera, Alexion/Portola, Boehringer Ingelheim (all fees paid to institution); is president of the Swiss Neurological Society.

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