



OPEN ACCESS

EDITED BY

Hans-Peter Hartung,
Heinrich Heine University, Germany

REVIEWED BY

Petia Dimova,
University Hospital St. Ivan Rilski, Bulgaria
Erdem Tüzün,
Istanbul University, Türkiye
José Fidel Baizabal-Carvallo,
University of Guanajuato, Mexico

*CORRESPONDENCE

Caio César Diniz Disserol
✉ caiodisserol@gmail.com

[†]These authors have contributed equally to this work

RECEIVED 11 July 2023

ACCEPTED 20 September 2023

PUBLISHED 19 October 2023

CITATION

Disserol CCD, Kowacs DP, Nabhan SK, Teive HAG and Kowacs PA (2023) Case report: Successful autologous hematopoietic stem cell transplantation in a patient with GAD antibody-spectrum disorder with rapidly progressive dementia.

Front. Neurol. 14:1254981.

doi: 10.3389/fneur.2023.1254981

COPYRIGHT

© 2023 Disserol, Kowacs, Nabhan, Teive and Kowacs. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Case report: Successful autologous hematopoietic stem cell transplantation in a patient with GAD antibody-spectrum disorder with rapidly progressive dementia

Caio César Diniz Disserol^{1,2*†}, Dora Pedroso Kowacs^{1†}, Samir Kanaan Nabhan^{3†}, Hélio Afonso Ghizoni Teive^{2†} and Pedro André Kowacs^{1,2†}

¹Department of Neurology, Instituto de Neurologia de Curitiba, Curitiba, Brazil, ²Department of Neurology, Complexo do Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, Brazil, ³Blood and Marrow Transplantation Program, Hospital de Clínicas, Federal University of Paraná, Curitiba, Brazil

The prevalence of neurological syndromes associated with antibodies to glutamic acid decarboxylase is increasing. While cognitive impairment is a common feature of this condition, it seldom emerges as the primary symptom. In this study, we discuss a case of refractory dementia associated with the glutamic acid decarboxylase spectrum disorder. Interestingly, this case showed a favorable outcome following autologous hematopoietic stem cell transplantation. We also provide an in-depth review of the current literature on the use of this therapeutic approach for the treatment of this disease.

KEYWORDS

autoimmune diseases of the nervous system, dementia, encephalitis, glutamic acid decarboxylase, neurocognitive disorders

Introduction

The range of neurological syndromes associated with antibodies to glutamic acid decarboxylase (GAD) continues to expand. Documented syndromes encompass stiff-person syndrome (SPS), ataxia, limbic encephalitis, epilepsy, nystagmus, and myoclonus (1). Cognitive impairment frequently appears in association with these syndromes (2), and isolated, rapidly progressive dementia has been observed (3). Collectively, these syndromes are now designated as GAD antibody-spectrum disorders (GAD-SDs) (1).

Treatment of GAD-SDs primarily involves pharmacological interventions to alleviate symptoms, complemented by immunotherapy. The majority of clinical evidence supporting immunotherapy is drawn from studies focused on patients with stiff-person syndrome, as SPS remains the most commonly diagnosed manifestation of GAD-SD. Thus, therapeutic strategies for other GAD-SDs are often derived from these data. The primary immunotherapy employed is intravenous immunoglobulin (IVIg) because of its proven efficacy in SPS. Other immunotherapeutic modalities with variable success include plasmapheresis, corticosteroids,

TABLE 1 Comparative table of formal neuropsychological assessments (pre- and post-HSCT).

Test	A*	B*	C*	Comparison* C x A or C x B
	April 2015	August 2015	March 2023	
Values in Z score				Difference $\geq 0,5$ DP
RAVLT - A1-A5 ¹	-0.3	-1.25	-0.7	Improvement (C > B)
RAVLT - A6 ²	0	-0.29	-0.2	No change (C = A; C = B)
RAVLT - A7 ³	0	-0.58	-0.5	No change (C = A; C = B)
WMS - LM I ⁴	0	-0.3	0.3	Improvement (C > B)
WMS - LM II ⁵	-0.3	0	0.7	Improvement (C > A; C > B)
CFT - Copy ⁶	2.5	2.5	2.5	No change (C = A; C = B)
CFT - Immediate ⁷	-0.5	0.1	-0.1	No change (C = A; C = B)
CFT ⁷ - Delay ⁸	0.4	-0.05	-0.05	No change (C = A; C = B)
WAIS-R ⁹ - Digit Span	-0.3	-2	-0.6	Improvement (C > B)
WAIS-R ⁶ - Information	0	0.3	0.3	No change (C = A; C = B)
WAIS-R ⁶ - Vocabulary	-0.6	-0.3	-0.3	No change (C = A; C = B)
WAIS-R ⁶ - Similarities	0	0.7	0.7	Improvement (C > A)
WAIS-R ⁶ - Arithmetic	0	-0.3	0.3	Improvement (C > A)
WAIS-R ⁶ - Pict. Comp. ¹⁰	-1.7	-	0.7	Improvement (C > A)
WAIS-R ⁶ - Block Design	-	-0.6	-0.3	Improvement (C > A)
WAIS-R ⁶ - L-N ¹¹	-0.3	-	1	Improvement (C > A)
WAIS-R - Digit Symbol-Coding	-0.3	-2	-0.6	Improvement (C > B)
Five-point Test	-1.5	-2	-0.3	Improvement (C > A; C > B)

No 2023 test scores decreased in comparison with scores from previous assessments.

¹RAVLT - A1-A5: Rey Auditory Verbal Learning Test - Learning curve: tests A1 to A5. ²RAVLT - A6: immediate recall (after distraction list B1, not presented here). ³RAVLT - A7: delayed recall (after 20 min). ⁴WMS-LM I- Wechsler Memory Scale - Logical Memory I subtest: immediate recall. ⁵WMS-LM II: delayed recall. ⁶CFT: Rey-Osterieth Complex Figure Copy: immediate copy for posterior reproduction. ⁷CFT: immediate reproduction (3' after copying). ⁸CFT: delayed reproduction (30' after copying). ⁹WAIS-R: Wechsler Adult Intelligence Scale - Revised.

¹⁰Pict. Comp.: WAIS-R Picture Completion subtest. ¹¹L-N: WAIS-R Letter-Number subtest.

and immunosuppressants. For patients who are resistant to these therapies, hematopoietic stem cell transplantation (HSCT) may be promising (1, 4).

In this paper, we discuss a patient who presented with rapidly progressive dementia and later manifested other GAD-SD symptoms. Despite being resistant to multiple immunotherapies, the patient responded positively to HSCT. Additionally, we provide a review of GAD-SD cases in the literature that have undergone HSCT treatment.

Case description

A 50-year-old woman, who had been a bank branch manager, sought medical attention in February 2015 due to a recent onset of forgetfulness. Over a period of weeks, she struggled with memorizing passwords and phone numbers, recognizing familiar clients, and performing work tasks. Within 2 months, she was experiencing frequent feelings of déjà vu. These symptoms, although fluctuating, progressively worsened, culminating in spatial disorientation that prevented her from leaving her home without assistance.

The patient's medical history included regular smoking, hypertension, ischemic heart disease, obstructive sleep apnea, and hypothyroidism. Neurological examinations revealed pronounced memory impairment, executive dysfunction, and visuospatial deficits. Comprehensive neuropsychological evaluations between April and

August 2015 confirmed this deterioration (Table 1, assessments A* and B*).

Initial blood work showed elevated glycated hemoglobin (HbA1c of 8.0%) but a standard metabolic panel, including thyroid function, vitamin B12, homocysteine, and folate levels. Serological tests for HIV, syphilis, and hepatitis were negative, and inflammatory markers were unremarkable. Although brain MRI and 18F FDG-PET scans were normal, EEG detected epileptiform discharges from the left temporal lobe. Investigations for autoimmune encephalopathies revealed significantly raised serum levels of anti-GAD (>2,000 IU/mL) and anti-ZnT8 (>500 IU/mL) antibodies, the latter being linked to type 1 diabetes. CSF analysis was typical, but anti-GAD antibodies were present. Other anti-neuronal antibody tests, both surface and intraneuronal, were negative. Neoplastic screening was unremarkable.

The patient was initially treated with methylprednisolone (1 g daily for 3 days) without improvement. Rituximab was then administered and adjusted based on the CD19 count. Despite a partial response and reduced serum anti-GAD levels, over the next 2 years, the patient developed left temporal lobe epilepsy, diabetes, ataxia, and stiff limb syndrome symptoms in her right leg. Intravenous immunoglobulin (IVIg) treatment was considered but was unavailable due to the COVID-19 pandemic. Azathioprine was tried unsuccessfully.

Recurrent episodes of isolated cognitive decline persisted. They were managed with high-dose corticosteroids, although symptom

relief seemed to stem mainly from the adjustment of symptomatic treatments. Three years into azathioprine treatment, the patient suffered a subacute decline in all GAD-SD symptoms that correlated with high serum anti-GAD levels. Azathioprine was halted, and although monthly low-dose IVIg was attempted, higher doses were denied by her health insurance. At this point, autologous hematopoietic stem cell transplantation (HSCT) was proposed.

Seven years after her initial symptoms (April 2022), the patient underwent HSCT. Despite post-transplant complications, such as treatment-resistant diarrhea due to pseudomembranous colitis, she displayed improvements in both physical and cognitive function (Figure 1, patient timeline). A follow-up neuropsychological assessment 10 months post-HSCT showed enhanced cognitive performance across various domains (Table 1, assessment C*). Subsequent brain MRIs and EEGs were standard. The patient regained many higher-level functions, managed her banking independently, and achieved better glycemic control, even discontinuing insulin use. Currently, her Modified Rankin Scale (mRs) score is 0, indicating no symptoms.

Discussion

“Dementia” refers to an acquired cognitive impairment in one or more cognitive domains. This decline from a previous level of functioning interferes with daily life activities and with an individual’s independence (5, 6). While neurodegenerative etiologies account for the majority of dementia cases (7), it is essential to identify potentially treatable causes (8, 9). Autoimmune etiologies should be considered, especially in instances with a rapidly progressive course, fluctuating symptoms, and the presence of seizures (9). It should be noted that these features are not exclusive. For example, rapidly progressive dementia can manifest in various diseases (10). Conditions like Lewy body disease, Parkinson’s disease, and vascular cognitive impairment

can exhibit fluctuating symptoms (11). Furthermore, seizures are commonly associated with dementia (12).

Rapidly Progressive Dementia (RPD) constitutes a small fraction of all dementias (3–4%). It is characterized by cognitive and functional impairments that manifest within 1–2 years, often within just weeks or months, as seen in our patient’s initial presentation (13). RPD can have different etiologies, with the most common being prion (a prototypical RPD), autoimmune, infectious, vascular, metabolic, neoplastic, and atypical manifestations of traditional degenerative diseases such as Alzheimer’s disease. Prompt evaluation is vital to identify potential treatable causes, such as autoimmune and inflammatory etiologies (10, 13).

The 1960s saw the first suspected descriptions of cognitive impairment due to autoimmune encephalitis. In 1966, Lord Brain chronicled a patient’s cognitive decline not associated with cancer (14). By 1968, Corsellis and colleagues had defined paraneoplastic limbic encephalitis as a distinct clinicopathological entity (15). Since then, our understanding of autoimmune encephalitis has grown exponentially, leading to the identification of numerous antineuronal antibodies (16), some of which cause dementia. Such cases are occasionally referred to as “autoimmune dementias” or “autoimmune encephalopathies” (9, 17). A study of 75 RPD cases over three years at a tertiary center identified 15 instances of an autoimmune nature, one of which was linked to anti-GAD antibodies (18). In the literature, we identified eight cases of anti-GAD dementia (refer to Table 2).

Glutamic acid decarboxylase (GAD) is an enzyme predominantly found in the central nervous system (CNS) and pancreatic beta cells. The first identification of autoantibodies targeting GAD dates back to 1988. In subsequent years, GAD antibodies have been linked to other clinical manifestations such as cerebellar ataxia, limbic encephalitis, myoclonus, and nystagmus. These varied clinical syndromes associated with GAD antibodies have been collectively categorized as “GAD antibody-spectrum disorders” (1).

Treatment strategies for GAD-SDs, excluding SPS, have not been universally agreed upon. However, intravenous

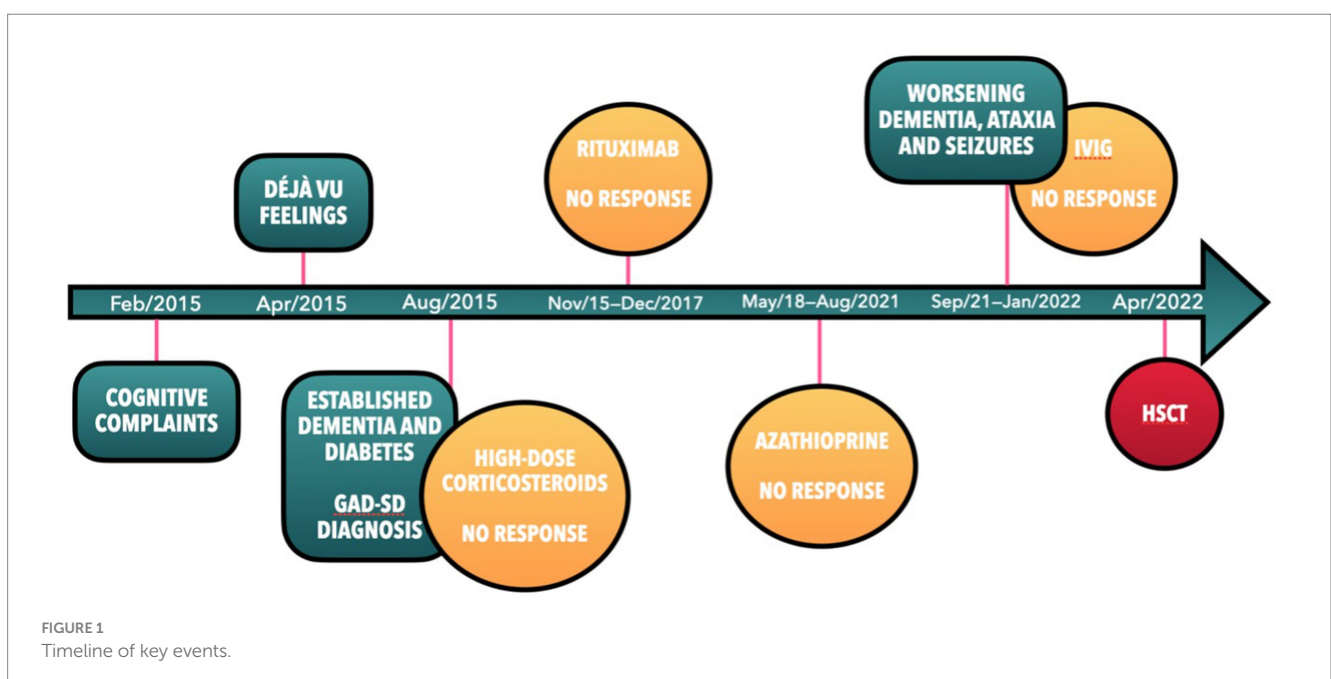


TABLE 2 Anti-GAD dementia cases.

Author	Year	n	Pre-treatment antibody titers	Treatment	Outcomes
Akkari et al. (19)	2021	1		IVIg	Improvement
Mirabelli-Badener et al. (20)	2012	1	Anti-GAD 641 U/mL (serum) Anti-Abs 154 pmol/L	Methylprednisolone + IVIg + Mycophenolate+ Rituximab	No improvement in symptoms. Only reduction in anti-GAD levels (<69 U/mL)
Markakis et al. (21)	2014	1	Anti-GAD 37,550 UI/mL (serum) 15,400UI/mL (liquor)	Methylprednisolone + PLEX+ Prednisolone	Symptom improvement and decrease in anti-GAD serum levels (9,600UI/mL)
Alencar et al. (22)	2017	1	Anti-GAD >100 U/mL (serum)	Methylprednisolone + IVIg + Glatiramer	Symptom improvement
Takagi et al. (23)	2011	1	Anti-GAD 2,865.2 U/mL (serum) (67.8 U/mL)	IVIg	No improvement in symptoms or reduction of antibody levels
Ren et al. (24)	2021	3	Anti-GAD 19,610UI/ml (serum) 3,325UI/mL (CSF) >300UI/mL (serum) >300 UI/mL (CSF) 3,400UI/mL (serum) 13UI/mL (CSF)	Methylprednisolone + IVIg + PLEX Methylprednisolone + IVIg Methylprednisolone + IVIg, Mycophenolato, Rituximabe, PLEX	Symptom improvement No improvement in symptoms Symptom improvement

GAD, gamma-aminobutyric acid decarboxylase; N, number; IVIg, intravenous immunoglobulin; PLEX, plasma exchange; MP, methylprednisolone; Anti-GAD serum levels, normal, <1 UI/mL - positive, >5 UI/mL - high, >= 2,000 UI/mL; Anti-GAD CSF levels, normal:<1 UI/mL- high:> 100 UI/mL.

TABLE 3 Autologous HSCT for anti-GAD spectrum disorders.

Author	Year	Condition (n)	Antibody titers (serum)	Previous treatment	Outcomes
Sanders et al. (26)	2014	SPS (2)	Anti-GAD: 5.6 and 127 Ui/mL	IVIg + Azathioprine + PLEX	Long-term remission
Kass-Iliyya et al. (27)	2021	SPS (3) PERM (1)	SPS pts.: Anti-GAD >2000 Ui/mL PERM pt.: Anti-GAD 372 Ui/mL + Anti-Gliadin positive + Anti- Glycine positive	IVIg +/- PLEX +/- Rituximab	All patients improved mobility and ambulation
Burt et al. (28)	2021	SPS (23)	Anti-GAD: 2,5 to >250 Ui/mL	IVIg +/- Rituximab or Azathioprine	17 responders (11 in remission for 3.5 years) – improvement in stiffness, spasms, mobility, and quality of life 6 non-responders

HSTC, hematopoietic stem cell transplantation; GAD, gamma-aminobutyric acid decarboxylase; (n), number of cases. SPS, stiff person syndrome; PERM, progressive encephalomyelitis with rigidity and myoclonus; EMG, electromyography; Cy, cyclophosphamide; G-CSF, granulocyte colony-stimulating factor; ATG, anti-thymocyte globulin; Anti-GAD 65, immunoprecipitation assay (IPA) / < ou igual a 0.02 nmol/L liquor; Anti-GAD -ELISA- serum level, POSITIVE > 10 UI/ML AND HIGH LEVEL > 100.000.

immunoglobulin (IVIg) is a prominently recognized modality, especially given its demonstrated efficacy in SPS patients (1, 25). The applicability of treatments across the range of GAD-SD manifestations remains an area of uncertainty, but current approaches seem plausible.

Recent literature has highlighted the potential for treating SPS using autologous hematopoietic stem cell transplantation (HSCT) (26–28). Cumulatively, these studies examined 29 patients who underwent HSCT (Table 3). While IVIg is a costly and long-term immunomodulatory strategy, autologous HSCT, despite its inherent risks, holds promise for

inducing prolonged remissions not only in GAD-SD but also in other neurological autoimmune disorders (29). Extensive consultations were held with our patient and her family regarding the potential benefits and risks of HSCT. The patient had expressed feelings of disappointment and depression stemming from the relentless progression of her disease and numerous unsuccessful treatments with conventional immunomodulatory and immunosuppressive strategies.

Autologous HSCT, as previously mentioned, is not without risks. Patients undergoing this procedure face potential threats from opportunistic infections and adverse reactions related to the drugs used (30). Notably, there is a documented case of a patient who developed severe anti-GAD encephalitis following an HSCT procedure (31). Additionally, other autoimmune conditions may emerge post-procedure (32). It is imperative that these considerations be meticulously weighed when recommending autologous HSCT to any patient diagnosed with GAD-SD. Nevertheless, our patient, fully aware of these risks, expressed that she would opt for the same course of treatment if faced with the decision again.

Conclusion

There is a broad spectrum of neurological conditions that can manifest as rapidly progressive dementia. Among these, autoimmune dementias, such as those presenting as GAD-SD, should always be on the differential list. Accurate diagnosis is pivotal, as it can guide appropriate treatment. In instances where patients are unresponsive to initial immunotherapies, consideration of HSCT as a treatment option becomes crucial.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent from the patients/participants or patients/participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

References

1. Tsiortou P, Alexopoulos H, Dalakas MC. GAD antibody-spectrum disorders: progress in clinical phenotypes, immunopathogenesis and therapeutic interventions. *Ther Adv Neurol Disord.* (2021) 14:175628642110034. doi: 10.1177/17562864211003486
2. Newsome SD, Johnson T. Stiff person syndrome spectrum disorders; more than meets the eye. *J Neuroimmunol.* (2022) 369:577915. doi: 10.1016/j.jneuroim.2022.577915
3. Mahale RR, Rajeevan S, Sivaprakash S, Padmanabha H, Mailankody P, Mathuranath P. Anti-GAD antibodies associated autoimmunity presenting as isolated dementia: an expansion of GAD antibody-spectrum disorders. *Acta Neurol Belg.* (2022) 123:657–9. doi: 10.1007/s13760-022-01937-w
4. Dalakas MC. Stiff-person syndrome and GAD antibody-spectrum disorders: GABAergic neuronal excitability, immunopathogenesis and update on antibody therapies. *Neurotherapeutics.* (2022) 19:832–47. doi: 10.1007/s13311-022-01188-w
5. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR, Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement.* (2011) 7:263–9. doi: 10.1016/j.jalz.2011.03.005
6. American Psychiatric Association. *DSM-5 task force. Diagnostic and statistical manual of mental disorders: DSM-5.* Virginia: American Psychiatric Association (2013). 947 p.

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

CD: Conceptualization, Writing – original draft, Writing – review & editing. DK: Conceptualization, Writing – original draft, Writing – review & editing. SN: Conceptualization, Writing – review & editing. HT: Conceptualization, Writing – review & editing. PK: Conceptualization, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Acknowledgments

The authors express their thankfulness to Dr. Livia Almeida Dutra, for debating the case; to the Brazilian Autoimmune Encephalitis Network, for their role on research in autoimmune encephalitis; and to André Pedroso Kowacs and Michael Wittelsbach Brochonski, for their review of style.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

7. Dintica CS, Yaffe K. Epidemiology and risk factors for dementia. *Psychiatr Clin N Am.* (2022) 45:677–89. doi: 10.1016/j.psc.2022.07.011
8. Geldmacher DS. Differential diagnosis of dementia syndromes In: GM Harper, editor. *Clinics in geriatric medicine*, vol. 20. Philadelphia, PA: W.B. Saunders (2004). 27–43.
9. Banks SA, Sechi E, Flanagan EP. Autoimmune encephalopathies presenting as dementia of subacute onset and rapid progression. *Ther Adv Neurol Disord.* (2021) 14:175628642199890. doi: 10.1177/1756286421998906
10. Hermann P, Zerr I. Rapidly progressive dementias — aetiologies, diagnosis and management. *Nat Rev Neurol.* (2022) 18:363–76. doi: 10.1038/s41582-022-00659-0
11. Matar E, Shine JM, Halliday GM, Lewis SJG. Cognitive fluctuations in Lewy body dementia: Towards a pathophysiological framework. *Brain.* (2020) 143:31–46. doi: 10.1093/brain/awz311
12. Zhao B, Shen LX, Ou YN, Ma YH, Dong Q, Tan L, et al. Risk of seizures and subclinical epileptiform activity in patients with dementia: A systematic review and meta-analysis. *Ageing Res Rev.* (2021) 72, 72. doi: 10.1016/j.arr.2021.101478
13. Day GS, Lazar E, Ghayal NB, Roemer SF, Graff-Radford NR, Dickson DW. Dissecting the neuropathological contributors to rapidly progressive dementia. *Alzheimer Dementia.* (2022) 18:e067009. doi: 10.1002/alz.067009
14. Oxon D, Eh JDO, Ball Lond K. Hashimoto's disease and encephalopathy lord brain. *Br Med J.* (1957) 62:1374.
15. Corsellis JAN, Goldberg GJ, Norton AR. Limbic encephalitis and its association with carcinoma [internet]. Available at: <http://brain.oxfordjournals.org/>
16. Dalmau J, Graus F. Antibody-mediated encephalitis. *N Engl J Med.* (2018) 378:840–51. doi: 10.1056/NEJMra1708712
17. Leypoldt F, Armangue T, Dalmau J. Autoimmune encephalopathies. *Ann N Y Acad Sci.* (2015) 1338:94–114. doi: 10.1111/nyas.12553
18. Neto AS, Soares Neto HR, Simabukuro MM, DJF Solla, MRR Gonc Alves, Fortini I, et al. Rapidly progressive dementia: prevalence and causes in a neurologic unit of a tertiary Hospital in Brazil [Internet]. (2016). Available at: www.alzheimerjournal.com
19. Akkari M, Messelmani M, Souissi W, Derbali H, Mrissa R. Subacute dementia revealing a limbic encephalitis with anti-GAD 65 antibodies in a young woman. *Acta Neurol Belg.* (2021) 122:1651–2. doi: 10.1007/s13760-021-01766-3
20. Mirabelli-Badenier M, Morana G, Pinto F, Uccelli A, Veneselli E, Battaglia FM, et al. Anti-glutamic acid decarboxylase limbic encephalitis without epilepsy evolving into dementia with cerebellar ataxia. *Arch Neurol.* (2012) 69:1064–6. doi: 10.1001/archneurol.2012.234
21. Markakis I, Alexopoulos H, Pouloupoulou C, Akrivou S, Papathanasiou A, Katsiva V, et al. Immunotherapy-responsive limbic encephalitis with antibodies to glutamic acid decarboxylase. *J Neurol Sci.* (2014) 343:192–4. doi: 10.1016/j.jns.2014.05.032
22. Alencar J, Ribeiro T, Diniz D, Melo G, Bezerra I, Junior R, et al. Anti-GAD positive autoimmune encephalitis presenting with dementia, psychiatric symptoms and MS findings on the MRI: a case report. *J Neurol Sci.* (2017) 381:536. doi: 10.1016/j.jns.2017.08.3720
23. Takagi M, Yamasaki H, Endo K, Yamada T, Kaneko K, Oka Y, et al. Cognitive decline in a patient with anti-glutamic acid decarboxylase autoimmunity; case report. *BMC Neurol.* (2011) 11:11. doi: 10.1186/1471-2377-11-156
24. Ren C, Ren H, Ren X, Zhang W, Li J, Dai L, et al. Case report: autoimmune encephalitis associated with anti-glutamic acid decarboxylase antibodies: a Pediatric case series. *Front Neurol.* (2021) 12:12. doi: 10.3389/fneur.2021.641024
25. Arinos M, Alakas CD, Ujii AF, Ashar B, Ufii L, Oan J, et al. The new England journal of medicine high-dose intravenous immune globulin for stiff-person syndrome a bstract background stiff-person syndrome is a disabling. *N Engl J Med.* (2001) 345 Available at: www.nejm.org
26. Sanders S, Bredeson C, Pringle CE, Martin L, Allan D, Bence-Bruckler I, et al. Autologous stem cell transplantation for stiff person syndrome: two cases from the Ottawa blood and marrow transplant program. *JAMA Neurol.* (2014) 71:1296–9. doi: 10.1001/jamaneurol.2014.1297
27. Kass-Iliyya L, Snowden JA, Thorpe A, Jessop H, Chantry AD, Sarrigiannis PG, et al. Autologous haematopoietic stem cell transplantation for refractory stiff-person syndrome: the UK experience. *J Neurol.* (2021) 268:265–75. doi: 10.1007/s00415-020-10054-8
28. Burt RK, Balabanov R, Han X, Quigley K, Arnautovic I, Helenowski I, et al. Autologous hematopoietic stem cell transplantation for stiff-person Spectrum disorder: a clinical trial. *Neurology.* (2021) 96:e817–30. doi: 10.1212/WNL.00000000000011338
29. Jaime-Pérez JC, Meléndez-Flores JD, Ramos-Dávila EM, González-Treviño M, Gómez-Almaguer D. Hematopoietic stem cell transplantation for uncommon immune-mediated neurological disorders: A literature review. *Cytotherapy.* (2022) 24:676–85. doi: 10.1016/j.jcyt.2021.12.006
30. Bazinet A, Popradi G. A general practitioner's guide to hematopoietic stem-cell transplantation. *Curr Oncol.* (2019) 26:187–91. doi: 10.3747/co.26.5033
31. Nagai K, Maekawa T, Terashima H, Kubota M, Ishiguro A. Severe anti-GAD antibody-associated encephalitis after stem cell transplantation. *Brain and Development.* (2019) 41:301–4. doi: 10.1016/j.braindev.2018.10.006
32. Burt RK, Muraro PA, Farge D, Oliveira MC, Snowden JA, Saccardi R, et al. New autoimmune diseases after autologous hematopoietic stem cell transplantation for multiple sclerosis. *Bone Marrow Transplant.* (2021) 56:1509–17. doi: 10.1038/s41409-021-01277-y