International Medical Case Reports Journal

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

Reversal of Cerebral Glucose Hypometabolism in a Patient with COVID and Refractory B-Cell Lymphoma

Lorvens Decosma[1], Emily Wolf[2], Ephraim E Parent[3], Han W Tun[2]

[1]Department of Internal Medicine, Mayo Clinic, Jacksonville, FL, USA; [2]Department of Hematology/Oncology, Mayo Clinic, Jacksonville, FL, USA; [3]Department of Radiology, Mayo Clinic, Jacksonville, FL, USA

Correspondence: Han W Tun, Department of Hematology/Oncology, Mayo Clinic, 4500 San Pablo Road S, Jacksonville, FL, 32224, USA, Email Tun.Han@mayo.edu

International Medical Case Reports Journal downloaded from https://www.dovepress.com/
For personal use only.

Abstract: Cerebral glucose hypometabolism (CGHM) involves reduced brain glucose uptake on FDG-PET imaging and occurs in neurological and systemic diseases. Its reversibility remains uncertain. We describe a 40-year-old man with reversible global CGHM associated with cryptogenic organizing pneumonia (COP) and COVID-19. His neurocognitive symptoms improved rapidly following steroid-induced hyperglycemia, with FDG-PET demonstrating complete CGHM resolution after two months. His medical background included primary refractory transformed follicular lymphoma diagnosed 30 months earlier, managed with multiple treatment regimens including CAR-T therapy. After post-CAR-T relapse, combination therapy with polatuzumab vendotin, bendamustine, and obinutuzumab achieved complete remission, which was maintained when CGHM developed. This case establishes that CGHM can be temporary and reversible, highlighting a previously unrecognized pathway through which systemic illness may produce neurocognitive impairment. The rapid cognitive recovery coinciding with steroid-induced hyperglycemia and COP treatment is significant. Additional investigation is warranted to determine CGHM's significance in diverse pathological conditions and determine therapeutic interventions.

Keywords: CGHM, lymphoma, prednisone, hyperglycemia, PET-CT imaging

Introduction

Positron emission tomography with [^{18}F]fluoro-2-deoxy-D-glucose (FDG–PET) is a well-established functional imaging modality for lymphoma staging and assessment of treatment response.[1] Cerebral glucose hypometabolism (CGHM) is defined as a significant decrease in glucose uptake in the brain on FDG-PET. It has been associated with neurological disorders such as neurodegenerative disorders as well as non-neurological systemic diseases including malignancies, hypoglycemic encephelopathy, depressive pseudodementia, and COVID-19 infection.[2–7] MRI studies of the brain have shown cerebral changes in cases of neurodegenerative disorders with CGHM indicating neuronal damage and loss.[2] However, cerebral changes are not consistently shown by MRI in patients with CGHM associated with non-neurological systemic diseases indicating the absence of neuronal damage or loss. The underlying mechanism of CGHM associated with non-neurological diseases is likely related to increased systemic glucose uptake acting as a glucose sink or interference with glucose uptake by neurons via immunological mechanisms. Association of CGHM with aggressive B cell lymphomas in the absence of CNS involvement is well-known.[3] CAR-T therapy used for hematologic malignancies has also been associated with CGHM which represents a novel mechanism for neurotoxicity.[8] As CGHM associated with non-neurological systemic diseases is not typically associated with cerebral involvement or damage, it is potentially reversible. An anecdotal report suggests clinical resolution of CGHM-associated neuro-psychiatric manifestations with glucose supplementation.[9] We report a case of transient and reversible CGHM associated with severe systemic inflammation secondary to COP and COVID-19 based on clinical as well as radiologic evidence.

https://doi.org/10.2147/IMCRJ.S603559
Received: 14 February 2026
Accepted: 13 May 2026
Published: 3 June 2026

© 2026 Decosma et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v4.0) License (http://creativecommons.org/licenses/by-nc/4.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

Case

The patient is a 40-year-old male with history of primary refractory, transformed follicular lymphoma (tFL) diagnosed in July 2021. He did not achieve complete remission following the initial treatment with six cycles of chemoimmunotherapy with R-CHOP (rituximab, cyclophosphamide, doxorubicine, vicristine, and prednisone). He went on to receive maintenance rituximab therapy but had rapid progression. Repeat biopsy of a lymph node showed findings consistent with tFL. He was treated with two cycles of obinutuzumab and ICE (ifosfamide, carboplatin, and etoposide) without significant response. He had CAR-T therapy without major cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS) in January 2023. FDG-PET in Feb and April 2023 showed complete response. Unfortunately, FDG-PET in September 2023 showed a major relapse.

He had two cycles of polatuzumab vendotin, bendamustine, and obinutuzumab in September and October 2023. The treatment was interrupted by COVID-19 infection with severe cough and shortness of breath and imaging findings consistent with pneumonia. He remained persistently positive for COVID-19 with no major improvement in respiratory symptoms. Early December 2023, he developed neurocognitive manifestations including confusion, poor memory, difficulty concentrating, difficulty with speech, and low mood. He described his status as having severe brain fog. FDG-PET in December 2023 showed no evidence of lymphoma but showed new bilateral lung opacities and global CGHM (Figure 1). Blood glucose on the day of FDG-PET was 143 mg/dl. Oxygen saturation was 100%, and he was intermittently febrile up to 103℉. C-reactive protein was exceptionally elevated at 168 (<5.0 mg/L). He underwent pulmonary consultation with bronchoscopy and bronchoalevolar lavage given the findings of bilateral lung opacities. Bacterial, fungal, and mycobacterial cultures were negative. Pneumocystis, cytomegalovirus, histoplasma, and blastomyces PCR testing was negative. Aspergillus antigen, legionella culture, nocardia stain, acid fast smear, and fungal smear were negative. Given the negative

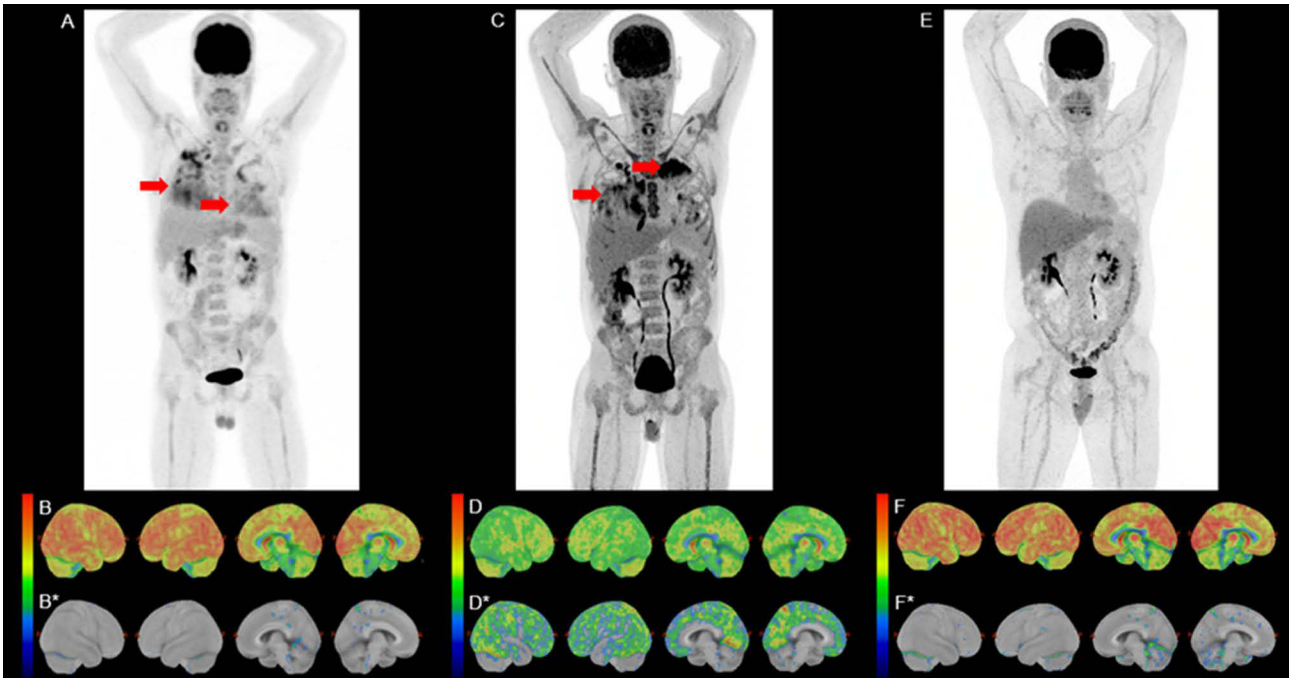

Figure 1 Reversible global cerebral hypometabolism on serial 18F-FDG PET. Whole body maximum intensity projection (MIP) and 3-D surface rendering of brain 18F-FDG uptake of man with refractory transformed follicular lymphoma and reversible cerebral glucose hypometabolism. At time of initial 18F-FDG PET imaging shown, the patient was noted to be in complete remission approximately one year after CAR-T and systemic targeted therapy but had developed COVID-19 pneumonia as shown on the18F-FDG MIP (red arrows) (**A**). 3-D 18F-FDG PET brain metabolism surface rendering using dedicated imaging software (GE AW server 3.2 with Cortex ID, MIM Neuro, version 7.2.7) shows relatively normal visual global metabolism (**B**) and no focal or global hypometabolism when compared to age and gender matched normal cohort in the database (**B***). Three months later, the patient presented with confusion and impaired memory in conjunction with worsening COVID-19 associated cryptogenic organizing pneumonia (COP) as seen on whole body imaging (red arrows) and no evidence of recurrent lymphoma (**C**). 3-D 18F-FDG PET brain surface rendering at that time demonstrated visual evidence of severe global cerebral hypometabolism (**D**) and statistical hypometabolism when compared to aged-normalized controls (**D***). Subsequently, patient was started on prednisone with rapid reversal of his neurocognitive symptoms and subsequent 18F-FDG PET demonstrated resolution of pulmonary inflammation (**E**) and return to baseline normal brain metabolism (**F**) and aged-normalized control comparison (**F***).

https://doi.org/10.2147/IMCRJ.S603559

infectious work up and clinical presentation, a final diagnosis of cryptogenic organizing pneumonia (COP) was made likely related to COVID-19, lymphoma, and lymphoma treatments. He was initiated on high-dose prednisone resulting in hyperglycemia with glucose going up as high as 407 mg/dl. The patient and the spouse reported rapid clearing of his neurocognitive symptoms within a few days after initiation of prednisone. He was initiated on insulin for steroid-induced hyperglycemia. The clearance of neuro-cognitive symptoms happened before the initiation of insulin. FDG-PET in February 2024 showed complete resolution of CGHM, improvement in pulmonary findings, and no evidence of lymphoma. He was further treated for COP with prednisone, mycophenolate mofetil, and IVIG with significant improvement in his respiratory status. FDG-PET in June 2024 showed resolution of hypermetabolic ground glass opacities, no evidence of lymphoma, and no evidence of CGHM (Figure 1). He had an unrelated donor allogeneic stem cell transplant soon after. At the time of writing, lymphoma remains in complete remission. He has not had any recurrence of neuro-cognitive symptoms. COP remains under control with low-dose prednisone and mycophenolate mofetil.

Discussion

Our report is likely the first report in literature clinically and radiologically capturing the transient and reversible nature of CGHM associated with a systemic non-neurologic disease state. We hypothesize the CGHM in our patient is likely secondary to severe systemic inflammation secondary to COP and COVID-19. While lymphoma is known to cause CGHM, this was felt less likely in this case, as the patient was in complete remission at the time of diagnosis with CGHM. CAR-T therapy has been associated with CGHM.[8] However, it was performed about 11 months before the CGHM. Previous studies examining patients 2 to 12 months post-CAR-T therapy have generally not detected significant long-term neurotoxicity or cognitive impairment from CAR-T therapy, suggesting CRS and ICANS appear shortly after treatment.[10] As such, CAR-T therapy is likely non-contributory in our patient. Moreover, FDG-PET scans performed around the time of CAR-T therapy did not show any evidence of CAR-T therapy related to CGHM.

Basic molecular mechanisms of CGHM have not been definitively elucidated. In neurological disorders such as neurodegenerative disorders, brain tumors, neurotoxic treatments such as brain radiation, CGHM is likely related to neuronal damage and loss.[2,11] A different mechanism is likely playing a role in CGHM associated with non-neurologic systemic diseases. The mechanism is possibly immunologic via cytokines and inflammatory mediators interfering with glucose uptake by neurons. Immune cells especially innate immune cells have been shown to express GLUT-3 which is also utilized by neurons for glucose uptake.[12] Aggressive malignant lymphocytes have been shown to express GLUT-3.[13] Thus, CGHM may develop secondary to the increased systemic glucose utilization created by severe inflammation and aggressive lymphomas. In CAR-T therapy setting, we have found a direct correlation between CGHM and ICANs suggesting that CGHM is likely immunologically mediated.[8] Neurologic symptoms including alterations in cognition, smell and taste impairment, headache, and seizure are prevalent in patients with COVID-19.[14] In a cohort of hospitalized COVID-19 patients who developed neurologic symptoms, FDG-PET demonstrated predominant frontoparietal hypometabolism in 10 of 15 patients.[15] The authors postulate that systemic cytokine-related inflammation leads to cortical dysfunction and cerebral hypometabolism.[15] In our patient, our hypothesis is that CGHM is likely secondary to shunting of glucose created by severe systemic inflammation associated with COP and COVID-19.

In terms of therapeutic interventions for CGHM associated with systemic diseases, treating the associated systemic disease is likely important. The resolution of CGHM in our patient is likely due to resolution of severe systemic inflammatory state. Moreover, glucose supplementation may be important. Rapid resolution of neurocognitive manifestations in our patient with the onset of steroid-induced hyperglycemia is quite interesting in that glucose supplementation can potentially help. Our group previously published a case in which neuro-psychiatric manifestations of lymphoma associated CGHM resolved with aggressive glucose supplementation even in the face of relentless progression of lymphoma.[9] Corticosteroids may have additional utility in the treatment of CGHM by modulating immune pathways through anti-inflammatory effects. It is also important to consider that the timing of corticosteroid treatment may have been coincidental, and the acute COVID-19 infection could have resolved independently. A reported case of post-acute COVID-19 described persistent cognitive deficits with corresponding abnormalities in brain glucose metabolism on FDG-PET, suggesting that CGHM may reflect prolonged or incomplete recovery after infection.[6] In contrast, our patient experienced rapid clinical and radiographic resolution, supporting the notion that CGHM can also be transient and reversible in acute systemic illness.

In conclusion, we suggest that CGHM represents a novel mechanism for neuro-cognitive manifestations in various systemic disease states. With more widespread use of FDG-PET, more cases of CGHM may become detected. From neuroradiology standpoint, detailed attention to the metabolic activity in the brain is necessary to diagnose CGHM. Standardized FDG-PET criteria for CGHM should be established. We demonstrated resolution of CGHM in this case with improvement in neurocognitive symptoms with corticosteroid treatment. It is not clear whether the reversal of CGHM was due to hyperglycemia or suppression of inflammation. Further research with collaboration across multiple institutions would be necessary to better understand CGHM.

Ethics Statement

This report describes a single clinical case and does not constitute human subjects research; therefore, Institutional Review Board approval was not required. In accordance with institutional policy at the Mayo Clinic, additional approval for publication of this case report was not required. Written informed consent for publication of case details and images was obtained from the patient.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Seam P, Juweid ME, Cheson BD. The role of FDG-PET scans in patients with lymphoma. *Blood J Am Soc Hematol*. 2007;110(10):3507–3516.
2. Mosconi L, Pupi A, De Leon MJ. Brain glucose hypometabolism and oxidative stress in preclinical Alzheimer's disease. *Ann NY Acad Sci*. 2008;1147(1):180–195. doi:10.1196/annals.1427.007
3. Hanaoka K, Hosono M, Shimono T, et al. Decreased brain FDG uptake in patients with extensive non-Hodgkin's lymphoma lesions. *Ann Nuclear Med*. 2010;24(10):707–711. doi:10.1007/s12149-010-0415-5
4. Guedj E, Campion J, Dudouet P, et al. 18F-FDG brain PET hypometabolism in patients with long COVID. *Eur J Nucl Med Mol Imaging*. 2021;48(9):2823–2833. doi:10.1007/s00259-021-05215-4
5. Shen XZ, Zhang YX, You QY. Case report of 18F-FDG PET/CT features of hypoglycemic encephalopathy. *Medicine*. 2023;102(24):e34025. doi:10.1097/MD.0000000000034025
6. Rossi S, Prodi E, Morese R, Paone G, Ruberto T, Sacco L. Persistent 18F-FDG brain PET fronto-temporal hypometabolism and cognitive symptoms two years after SARS-CoV-2 infection: a case report. *Neurol Int*. 2023;15(3):908–916. doi:10.3390/neurolint15030058
7. Pozzi FE, Licciardo D, Musarra M, et al. Depressive pseudodementia with reversible AD-like brain hypometabolism: a case report and a review of the literature. *J Personalized Med*. 2022;12(10):1665. doi:10.3390/jpm12101665
8. Wolf E, Iqbal M, Li Z, Tun HW, Parent EE. Chimeric antigen receptor T-cell therapy associated cerebral glucose hypometabolism (CART-CGHM): a novel cerebral metabolic complication. *Blood*. 2024;144(Supplement 1):3418. doi:10.1182/blood-2024-206396
9. Kase AM, Bullock C, Parrondo R, et al. Neuropsychiatric manifestations of lymphoma-associated cerebral glucose hypometabolism can be reversed by intensive glucose supplementation. *Blood Lymphat Cancer*. 2022;12:17–21. doi:10.2147/BLCTT.S353430
10. Rubin DB, Danish HH, Ali AB, et al. Neurological toxicities associated with chimeric antigen receptor T-cell therapy. *Brain*. 2019;142(5):1334–1348. doi:10.1093/brain/awz053
11. Andersen PB, Krabbe K, Leffers AM, et al. Cerebral glucose metabolism in long-term survivors of childhood primary brain tumors treated with surgery and radiotherapy. *J Neuro-Oncol*. 2003;62(3):305–313. doi:10.1023/A:1023371424483
12. Fu Y, Maianu L, Melbert BR, Garvey WT. Facilitative glucose transporter gene expression in human lymphocytes, monocytes, and macrophages: a role for GLUT isoforms 1, 3, and 5 in the immune response and foam cell formation. *Blood Cells Mol Dis*. 2004;32(1):182–190. doi:10.1016/j.bcmd.2003.09.002
13. Xu Y, Zhou X, Zhang S, Nanding A, Xuan Q. Expression and prognostic value of glucose transporter 3 in diffuse Large b cell lymphoma. *Onco Targets Ther*. 2022;Volume 15:181–191. doi:10.2147/OTT.S338826
14. Misra S, Kolappa K, Prasad M, et al. Frequency of neurologic manifestations in COVID-19: a systematic review and meta-analysis. *Neurology*. 2021;97(23):e2269–e2281. doi:10.1212/WNL.0000000000012930
15. Hosp JA, Dressing A, Blazhenets G, et al. Cognitive impairment and altered cerebral glucose metabolism in the subacute stage of COVID-19. *Brain*. 2021;144(4):1263–1276. doi:10.1093/brain/awab009

International Medical Case Reports Journal

Dovepress
Taylor & Francis Group

Publish your work in this journal

The International Medical Case Reports Journal is an international, peer-reviewed open-access journal publishing original case reports from all medical specialties. Previously unpublished medical posters are also accepted relating to any area of clinical or preclinical science. Submissions should not normally exceed 2,000 words or 4 published pages including figures, diagrams and references. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/international-medical-case-reports-journal-journal