

CASE REPORT

I cannot picture it in my mind: acquired aphantasia after autologous stem cell transplantation for multiple myeloma

Adam L. Bumgardner¹, Kyle Yuan² and Alden V. Chiu^{3,4,*}¹Internal Medicine and Psychiatry Residency Program, National Capital Consortium, Bethesda, MD, USA, ²F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA,³Hematology-Oncology Service, Walter Reed National Military Medical Center, Bethesda, MD, USA,⁴Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

*Correspondence address. Hematology-Oncology Service, Walter Reed National Military Medical Center, Bethesda, MD 20889, USA. Tel: +1-301-319-2100; Fax: +1-301-319-2119; E-mail: alden.v.chiu.mil@mail.mil

Abstract

Aphantasia, the loss of mental imagery, is a rare disorder and even more infrequent when acquired. No previous cases have been identified that were caused by transplant-related treatment. We describe a case of acquired aphantasia in a 62-year-old male with refractory IgG kappa multiple myeloma after receiving an autologous stem cell transplant (ASCT) following high-dose melphalan with a complicated hospital admission. The etiology of aphantasia remains unidentified, but we provide viable explanations to include direct effects from ASCT treatment and indirect effects from transplant-related complications.

INTRODUCTION

Volitional imagery composition within one's thoughts is a complex neurological task that is inherently human. It has been described in literature under multiple terms including imagery phenomenology, mind's eye and visual imagery [1, 2]. Although mental imagery seems like a universal human ability, some people are incapable of it. Aphantasia is the term for an inability to visualize within one's mind's eye, which was created in 2015 by Zeman et al. [2, 3]. Two types have been described in the literature: acquired and congenital [1, 3, 4].

Case reports describing acquired aphantasia often include direct cerebral damage such as bilateral posterior cerebral artery (PCA) stroke [1] or left PCA stroke and a presumed anoxic episode [4]. Another case report details a patient without known direct neurologic insult who developed aphantasia after coronary angioplasty without any other cognitive deficits [2].

Here, we present a case of acquired aphantasia in a 62-year-old male with a history of IgG kappa multiple myeloma admitted for autologous stem cell transplant (ASCT) after high-dose melphalan who had a prolonged admission due to *Streptococcus mitis* bacteremia and presumed neutropenic enterocolitis.

CASE REPORT

The patient is a 62-year-old male with refractory IgG kappa multiple myeloma with t(11:14) admitted for his second ASCT with melphalan 200 mg/m².

On Day 0, the patient's stem cells were reinfused without any complications. Per hospital protocol, the patient was initiated on prophylactic valacyclovir and levofloxacin.

On Day 8, the patient was transferred to the intensive care unit for tachypnea, tachycardia and febrile neutropenia with

†Alden V. Chiu, <http://orcid.org/0000-0002-5494-4088>

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an absolute neutrophil count of zero. Fatigue was his main complaint and physical examination was unremarkable. Hospital course ultimately included a variety of antimicrobials including cefepime, doxycycline, meropenem, piperacillin/tazobactam, vancomycin and micafungin during stabilization efforts. He developed diarrhea and a CT scan of the abdomen demonstrated bowel wall thickening concerning for neutropenic enterocolitis. Blood cultures grew pan-sensitive *S. mitis*. Antibiotics were de-escalated to cefepime, metronidazole and vancomycin. His course was further complicated on Day 9 by a spontaneous pneumothorax, which developed after induced sputum samples were taken to rule out tuberculosis. Pneumothorax resolved after chest tube placement. He was discharged on Day 20 after neutrophil engraftment and resolution of infections.

On Day 9, the patient began to report an 'inability to picture things in my head when I close my eyes', and when he closed his eyes to see a recent meal or mentally practice his golf putts, he only pictured blackness. Using the modified vividness of visual imagery questionnaire (VVIQ), a series of 16 questions where participants rate how well they can visualize a prompt, he scored the lowest possible score of 16 [5] and was diagnosed with aphantasia. After returning from the ICU on Day 12, he reported subjective improvement of his aphantasia by seeing 'constantly morphing shapes when closing my eyes'. However, a repeat VVIQ performed the day prior to discharge remained 16.

During his 6-month follow up, he reported mild improvement but not resolution of aphantasia. His VVIQ was 23 at this time.

DISCUSSION

The paucity of literature on aphantasia, especially when acquired, limits our understanding of this rare disorder. Our patient had a complicated hospital course and there are numerous possible etiologies for his aphantasia which include the ASCT process, gut dysbiosis, hypoxemia and a psychogenic etiology.

High-dose melphalan with ASCT rescue has also been correlated with neurologic effects. A single-center longitudinal study involving 29 patients with multiple myeloma examined most common symptoms following this regimen during hospital admission and follow up in clinic [6]. Neurologic effects included fatigue, insomnia, anxiety, dysguesia and later manifestations of concentration and memory problems. Since higher order cognitive deficits are seen, areas in his brain responsible for imagery production may be affected. Timing is plausible given manifestation of aphantasia 1 week after reinfusion.

Dimethylsulfoxide (DMSO)—a stem cell cryopreservative—has been associated with neurologic effects during stem cell transplantation. An example is a 49-year-old male who developed a generalized tonic-clonic seizure within minutes after two ASCTs with DMSO and subsequent altered mental status [7]. It is possible but unlikely that this patient had a late complication due to DMSO causing aphantasia. Our patient had no other neurologic deficits or altered level of consciousness that were described in prior case presentations describing DMSO reactions.

Antibiotics can alter normal gastrointestinal flora, termed gut dysbiosis, which changes bacterial metabolites resulting in decreased neural signaling-related molecules [8]. An animal model studying mice were given 5 antibiotics for 11 days with results notable for decreased levels of short chain fatty acids, brain derived neurotrophic factor and neuropeptide Y. This translated to impaired novel object recognition. It is impossible to ascertain if the mice developed aphantasia but higher

cognitive functions within image recognition were likely disrupted. Our patient was treated with more than five antibiotics, which could have resulted in insufficient metabolites for proper neuronal function.

Anoxic brain injuries have been implicated as a cause of aphantasia albeit by stroke [4]. A pneumothorax causes hypoxemia through shunt physiology [9] and sepsis produces this by direct lung damage through cytokine-mediated alveolar capillary injury as well as oxidative and nitrosative stress [10]. Since our patient developed these almost concurrently with his mental imagery deficit, a hypoxic brain injury is considered the most likely etiology.

Lastly, there have been reports of psychogenic aphantasia [4]. A functional cause is possible, especially because the patient was under significant duress including bacteremia, possible neutropenic enterocolitis, an ICU transfer and a pneumothorax all after receiving ASCT for refractory multiple myeloma. His affect also acutely changed from bright and humorous to dysphoric and irritable requesting an early discharge before medically appropriate.

Given the evidence, we speculate the patient acquired aphantasia from a hypoxemic insult to the central nervous system. Due to the novelty of this neurologic deficit, a more extensive evaluation was not ordered at the time. This leaves room for some uncertainty as to the ultimate etiology and future evaluations should consider obtaining cerebrospinal fluid analysis, brain imaging, electroencephalograms and even functional magnetic resonance imaging during the evaluation.

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CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest.

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ETHICAL APPROVAL

The authors declare that no formal ethical approval was needed for this work.

CONSENT

The patient provided written informed consent on 22 April 2020 for the potential publication of this case report.

GUARANTOR

The guarantor is Dr. Alden Chiu.

REFERENCES

1. Thorudottir S, Sigurdardottir HM, Rice GE, Kerry SJ, Robotham RJ, Leff AP et al. The architect who lost the ability to imagine: the cerebral basis of visual imagery. *Brain Sci* 2020 Feb;10:59. doi: [10.3390/brainsci10020059](https://doi.org/10.3390/brainsci10020059).

2. Zeman AZ, Della Sala S, Torrens LA, Gountouna VE, McGonigle DJ, Logie RH. Loss of imagery phenomenology with intact visuo-spatial task performance: a case of 'blind imagination'. *Neuropsychologia* 2010 Jan 1;48:145–55. doi: [10.1016/j.neuropsychologia.2009.08.024](https://doi.org/10.1016/j.neuropsychologia.2009.08.024).
3. Zeman A, Dewar M, Della SS. Reflections on aphantasia. *Cortex* 2016 Jan 1;74:336–7. doi: [10.1016/j.cortex.2015.08.015](https://doi.org/10.1016/j.cortex.2015.08.015).
4. Farah MJ, Levine DN, Calvanio R. A case study of mental imagery deficit. *Brain Cogn* 1988 Oct 1;8:147–64. doi: [10.1016/0278-2626\(88\)90046-2](https://doi.org/10.1016/0278-2626(88)90046-2).
5. Fulford J, Milton F, Salas D, Smith A, Simler A, Winlove C et al. The neural correlates of visual imagery vividness—an fMRI study and literature review. *Cortex* 2018 Aug 1;105:26–40. doi: [10.1016/j.cortex.2017.09.014](https://doi.org/10.1016/j.cortex.2017.09.014).
6. Naegele M, Kirsch M, Ihorst G, Fierz K, Engelhardt M, De Geest S. Symptom experience of multiple myeloma (syMMex) patients treated with autologous stem cell transplantation following high-dose melphalan: a descriptive longitudinal study. *Support Care Cancer* 2018 Mar 1;26:833–41. doi: [10.1007/s00520-017-3897-z](https://doi.org/10.1007/s00520-017-3897-z).
7. Bauwens D, Hantson P, Laterre PF, Michaux L, Latinne D, De Tourtchaninoff M et al. Recurrent seizure and sustained encephalopathy associated with dimethylsulfoxide-preserved stem cell infusion. *Leuk Lymphoma* 2005 Jan 1;46:1671–4. doi: [10.1080/10428190500235611](https://doi.org/10.1080/10428190500235611).
8. Fröhlich EE, Farzi A, Mayerhofer R, Reichmann F, Jačan A, Wagner B et al. Cognitive impairment by antibiotic-induced gut dysbiosis: analysis of gut microbiota-brain communication. *Brain Behav Immun* 2016 Aug 1;56:140–55. doi: [10.1016/j.bbi.2016.02.020](https://doi.org/10.1016/j.bbi.2016.02.020).
9. Arshad H, Young M, Adurty R, Singh AC. Acute pneumothorax. *Crit Care Nurs Q* 2016 Apr 1;39:176–89. doi: [10.1097/cnq.0000000000000110](https://doi.org/10.1097/cnq.0000000000000110).
10. Hotchkiss RS, Moldawer LL, Opal SM, Reinhart K, Turnbull IR, Vincent JL. Sepsis and septic shock. *Nat Rev Dis Primers* 2016 Jun 30;2:1–21. doi: [10.1038/nrdp.2016.45](https://doi.org/10.1038/nrdp.2016.45).