

Postanesthesia Persistent Amnesia in a Patient With a Prior History of Dissociative Fugue State: The Case for the Two-Hit Hypothesis

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Case Presentation

The psychiatry service was called to evaluate a patient in the outpatient procedure unit who could not remember who she was or why she was there. “Ms. R” was a 36-year-old Hispanic woman with a history of morbid obesity who underwent an upper endoscopy for evaluation of nausea and inability to tolerate oral intake 1 month after a Roux-en-Y gastric bypass for her obesity. The endoscopy demonstrated moderate stenosis at the gastrojejunal anastomosis, which did not account for the severity of her nausea. The stenosis was dilated without incident. For the procedure, Ms. R received a total of 420 mg i.v. of propofol, 100 mg i.v. of lidocaine, and 0.2 mg i.v. of glycopyrrolate. She also received a total of 200 µg i.v. of phenylephrine for a transient decrease in blood pressure to 81/45. In the recovery room, when Ms. R awoke from her conscious sedation, she had no recollection of why she was in the hospital, was disoriented to place, and, most significantly, was unable to recall her identity. She was agitated, prompting the psychiatric consultation. Ms. R was visibly frightened when any person tried to approach her, including her boyfriend of 5 years. She repeatedly asked why she was there but was unable to retain the information received. She was given 2 mg of midazolam for agitation, after which a minor improvement in behavior was observed. A repeat dose of midazolam was administered, without further improvement. Forty-five minutes after the procedure, Ms. R was still unable to recall her date of birth. Her vital signs and general physical and neurological examination were within normal limits. Her mental status examination was significant for agitation, disorientation to person and place, and extensive memory loss, which continued for the rest of the day. She repeatedly expressed the delusion that the baby she had just delivered was taken from her. She had no evidence of hallucinations. A preprocedure pregnancy test was negative. Ms. R was on a liquid diet and taking a multivitamin once daily, 1,000 µg of vitamin B₁₂ three times a week sublingually, and calcium citrate daily.

Ms. R’s past medical history included a history of gallstones as well as the Roux-en-Y gastric bypass surgery

1 month earlier, at which time her body mass index (BMI) was 47. Ms. R had received 200 mg of propofol as part of the anesthesia during the 3-hour bariatric surgery without incident. Ursodiol was begun 3 weeks before the endoscopy for nausea that developed while she was consuming a postoperative liquid diet. When her diet was advanced to soft foods, she began vomiting. She returned to a liquid diet, and the endoscopy was scheduled. Ms. R’s past psychiatric history was significant for a dissociative fugue, which occurred at the same time as her divorce 7 years earlier and for which she was psychiatrically hospitalized. She continued in individual and group treatment for 2 years after that hospitalization. She had no history of traumatic events.

Because of Ms. R’s persistent amnesia and agitation, she was admitted to a medical unit for further evaluation. Results of all testing, routine laboratory tests, urine drug screen, head CT, head MRI, and EEG were normal except for ketones in the urine. Ms. R’s BMI had decreased to 40.5. She was started on a clear liquid diet and had no further nausea. The neurology consultant agreed with the psychiatrist’s diagnosis of dissociative amnesia. During her hospitalization, Ms. R slowly regained some of her memory. She vaguely remembered that she had an adult son living in another state. Ms. R could not remember how to use her cell phone. She was afraid to take a shower without supervision as she was not sure she would know what to do. She also could not recall important historical events, such as the September 2001 attacks on the World Trade Center. There was no evidence of anterograde amnesia after the first hospital day. After showing some improvement over her 6-day hospitalization, she was discharged home with her boyfriend.

Two weeks after hospital discharge, Ms. R continued to recover some of her memories and to increase her activities. It was unclear, however, whether her retrograde amnesia was improving or whether she was only retaining newly learned information. She began to cook on her own and reported increased comfort around her boyfriend and her family. Ms. R was afraid to return to work because she was concerned that she would not remember how to do her job. Within 2 months of the episode, Ms. R was retrained by her employer and successfully resumed her work as a secretary. Six months after the procedure, Ms. R’s retrograde amnesia had significantly improved and she continued to form new memories without difficulty.

Discussion

This case report underscores the importance of considering both the organic and the psychiatric precipitants of

an acute-onset persistent amnesia, and here we explore how anesthesia, recent gastric bypass, and emotional distress may be risk factors for dissociative amnesia.

To our knowledge, severe memory loss with prolonged retrograde amnesia after an upper endoscopy procedure has never before been reported in an adult. One case reported in the pediatric literature (1) described a 12-year-old boy with a history of attention deficit hyperactivity disorder who underwent upper endoscopy with propofol sedation and no intraoperative complications. After the procedure, the boy had difficulty with short-term recall. While he knew he was in the hospital, he could neither recall the reason he was there nor recognize his family. Gradual improvement in his memory was noted over time, but the boy did not feel that his memory had returned to baseline 6 months after the procedure. Another five children (S.A. Quraishi, personal communication, April 2012) between the ages of 7 and 17 years were evaluated for memory problems after undergoing induction of anesthesia with propofol. Like Ms. R, four of the six children had prolonged amnesia after propofol-induced sedation for endoscopy. All six children had an underlying psychiatric diagnosis for which they were receiving treatment, and five were receiving psychotropic medication. In general, propofol has been associated with anterograde amnesia and not retrograde amnesia (2). Thus, a small subset of children with psychiatric disorders may have an associated vulnerability to propofol-associated prolonged amnesia, especially when this agent is given rapidly, as in endoscopy (four children) and tooth extraction (two children).

Propofol has been associated with postoperative amnesia in adults. In a study of postoperative amnesia, 55 women scheduled to undergo cesarean section were randomly assigned to anesthesia with propofol or midazolam. After the operation, five of 30 new mothers who received propofol were unable to remember either meeting their baby or the sex of their baby. In contrast, all 25 of the new mothers who received midazolam (with flumazenil reversal) remembered meeting their baby and the baby's sex (3). As noted in our case presentation, Ms. R received midazolam in the recovery room, which may have exacerbated her confusion and amnesia. Midazolam can cause amnesia and is associated with a decrease in propofol clearance when administered simultaneously (4).

Global postoperative amnesia has been described in rare cases and was ruled out as a possibility in Ms. R's case because of the prolonged time course of her amnesia. Global postoperative amnesia has been attributed to transient global amnesia, a poorly understood condition that lasts only 24 hours or so (5). While prolonged amnesia following gastric bypass surgery has not been described in the literature, there have been several case reports of

significant short-term memory loss following gastric bypass surgery (6). In general, those patients had prolonged emesis, were diagnosed with Wernicke's encephalopathy, and demonstrated typical neurological manifestations, such as lateral gaze paralysis (7). Our patient had a week of emesis and no abnormal neurological findings. Therefore, this syndrome seemed unlikely to be the cause of her memory loss.

It is important to consider not just the physiological precipitants of this patient's amnesia, but also psychogenic causes. The term *psychogenic amnesia* describes a primary etiology of psychological stress without ignoring its neuroanatomical correlates. The use of terms such as *functional* or *hysterical memory loss* can be problematic and stigmatizing for patients (8). Of the types of psychogenic amnesia, the phenomenon of psychogenic fugue is perhaps the most psychologically determined. Psychogenic fugue is characterized by a sudden loss of all autobiographical memories and sense of personal identity. Factors that can contribute to a fugue include severe precipitating stress such as marital discord, financial problems, or emotional upheaval; depression; and organic causes, such as head injury. Notably, Ms. R did have

a previous history of psychogenic fugue, suggesting her vulnerability to psychogenic memory loss. Before her endoscopy-associated amnesia, she also had recent stressors in the form of financial struggles and relationship problems with her boyfriend.

Another approach to understanding the cause of memory loss as psy-

chological as opposed to organic is by the type of content that is affected. Traditionally, focal retrograde amnesia in the absence of anterograde amnesia has implied a psychogenic origin rather than a biological one. A further divide has been noted between retrograde amnesia for purely autobiographical data compared with a more global retrograde amnesia, which encompasses procedural memory (memory for how to perform tasks) and implicit memory (memory not requiring executive control, such as how to brush one's teeth) as well. While Ms. R did present primarily with focal retrograde amnesia for autobiographical information, she also displayed some symptoms of procedural memory loss, such as an inability to use her cell phone and uncertainty about how one takes a shower. The combination of procedural memory loss and the temporal relationship of her memory loss following upper endoscopy highlights the importance of allowing for both brain and psychological vulnerability to account for a dissociative amnesia. Hence, it may be most helpful in the case of Ms. R (and similar cases) to explain her presentation with a "two-hit" hypothesis. The interaction of these two hits could have been additive. Psychological stressors may sensitize predisposed patients to amnesia after administration

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of anesthetic agents such as propofol. It is also possible that an anesthetic-associated amnesia could have been prolonged by the appearance of the stress-linked partner in the recovery room. With the syndromes of psychogenic fugue and amnesia, there is increasing evidence that psychologically triggered memory repression is itself associated with an altered pattern of neural activity, particularly prefrontal cortex activation and hippocampal deactivation (9). Correspondingly, propofol-associated amnesia is also linked with hippocampal deactivation, via the basolateral amygdala (10).

This case integrates two seemingly separate causes of dissociative amnesia: psychological vulnerability and commonly used anesthetic agents. To our knowledge, this is the first report of prolonged amnesia after an endoscopy in an adult. Whether this represents a highly unusual case, exacerbated by the patient's psychological vulnerability, remains to be determined. Clinicians should be aware of the possibility of prolonged memory loss in patients with a previous history of dissociative episodes. Persistent amnesia is disabling, and amnesia associated with identity loss is extremely disruptive and upsetting. Further study of episodic memory loss, particularly using functional neuroimaging, should help elucidate the biological basis of amnesia, irrespective of its presumptive origin.

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Clinical Guidance: Prolonged Amnesia Following Anesthesia

Anesthetic agents, particularly propofol, may produce persistent memory loss in patients under severe psychological stress. Roberts et al. propose a “two-hit” explanation—multiple recent stressors plus propofol anesthesia—for the prolonged retrograde amnesia of a woman who underwent an upper endoscopy and afterward was unable to recall even her own identity. Seven years earlier she had experienced a dissociative fugue during a divorce, suggesting a vulnerability to psychogenic memory loss. Thus, a previous history of dissociative episodes may be a consideration in exposing patients to anesthetic agents.