CLINICAL PRACTICE

Exercises in Clinical Reasoning

Managing Cognitive Load to Uncover an Unusual Cause of Syncope: Exercises in Clinical Reasoning

Christopher Small, M.D.[1], *Andrew M. Land, M.D.*[1], *Steven A. Haist, M.D., M.S.*[2], *Carlos A. Estrada, M.D., M.S.*[3,4], *and Erin D. Snyder, M.D.*[1,3,4]

[1]Tinsley Harrison Internal Medicine Residency Program, University of Alabama at Birmingham, Birmingham, AL, USA; [2]National Board of Medical Examiners, Philadelphia, PA, USA; [3]Birmingham Veterans Affairs Medical Center, Birmingham, AL, USA; [4]University of Alabama at Birmingham, Birmingham, AL, USA.

KEY WORDS: clinical reasoning; cognitive load; hyperviscosity syndrome; syncope.
J Gen Intern Med 31(2):247–51
DOI: 10.1007/s11606-015-3534-9

In this series, a clinician extemporaneously discusses the diagnostic approach (regular text) to sequentially presented clinical information (bold). Additional commentary on the diagnostic reasoning process (italics) is integrated throughout the discussion.

CLINICAL INFORMATION

A 72-year-old man presented to the emergency department after a syncopal episode at home. For the past 2 months, he had syncope and near syncope with associated generalized weakness, nausea, scotomas, and subjective hearing loss. He sustained multiple falls during the episodes. His symptoms come on without warning, usually when he is changing positions. He did not describe vertigo or dizziness. A month prior, he was prescribed meclizine for these episodes, without any benefit.

CLINICIAN RESPONSE

Any time I think about a diagnosis with multiple potential etiologies, like syncope, I try to put possibilities in large and small "buckets." For example, the cardiovascular system is one of those "large buckets," in which one may find a lot of different causes of syncope. Some specific diagnoses include tachy- or brady-arrhythmias, along with etiologies related to valvular heart disease. Neurally induced causes are another "large bucket"; examples would include situational micturition and cough syncope. Finally, orthostatic syncope, due to obstruction or reduction of blood flow, would fall into a third "large bucket."

My next inquiries would include asking about the circumstances surrounding the syncope and presyncope. For example, was he urinating; did he exert himself beforehand; did he have any palpitations? Neurally induced causes such as vasovagal syncope often have associated dizziness or nausea. I would also want to know what he was like when he awoke from his episode.

CLINICAL REASONING

Syncope carries with it a long differential diagnosis that can sometimes seem overwhelming as a clinician gets started with a case. This overwhelming sensation is a symptom of excess cognitive load when faced with a complex problem. Short-term memory, can only hold 5–9 pieces of information at once, which are then presented to working memory.[1] *However, long-term memory capacity is nearly unlimited. Our clinician quickly deals with the complexity of the problem by utilizing a schema from his long-term memory to evaluate syncope. This schema, organizing potential diagnoses into "buckets," allows him to chunk multiple pieces of information together, thereby reducing the number of elements that his short term memory must hold at the same time.*[2] *Each bucket becomes a separate element that is presented to working memory. The clinician can then focus on each bucket individually, in order to get a grasp of the overall problem at hand.*

The discussant tries here to gather more information to better understand this patient's syncope as cardiogenic or neurally mediated, so as to know which "bucket" is more likely to hold the correct diagnosis.

CLINICAL INFORMATION

He was sitting at the time of the most recent event and sustained no injuries as a result of his fall. His roommate, who witnessed the event, saw no jerking or twitching. Afterward, the patient was mildly confused for 1–2 min and did not recall the events preceding the episode. During

Received May 7, 2015
Revised August 25, 2015
Accepted October 20, 2015
Published online November 5, 2015

his prior episodes, he was not urinating, defecating, or straining. He reported no palpitations or chest pain.

He reported a 40-pound weight loss during the six months prior to this episode. A month prior, he suffered a gastrointestinal bleed. A colonoscopy demonstrated internal hemorrhoids. He had no evidence of malignancy on either colonoscopy or upper endoscopy.

He has a history of diet-controlled diabetes mellitus, hypertension, hyperlipidemia, chronic kidney disease (stage IIIB), anemia from iron deficiency, insomnia, and long-standing B-12 deficiency. His home medications are losartan, ferrous sulfate, omeprazole, trazodone, monthly B-12 injections, and meclizine. He lives with three roommates locally. He smokes an occasional cigar but denies alcohol use. He has no known history of coronary artery disease, heart failure, or cardiac arrhythmia.

CLINICIAN RESPONSE

Certainly orthostasis from anemia due to his gastrointestinal bleeding becomes a possibility. Did his syncope precede the admission for gastrointestinal bleeding? When performing the physical examination, I would do a thorough cardiac exam, looking for signs of aortic stenosis, including non-valvular outflow obstruction. A thorough neurologic exam is also required in this setting. A focused evaluation directed by the history and physical exam can be much more efficient and cost-effective than the diagnostic testing typically recommended for patients with syncope, as it is expensive and often not helpful.

CLINICAL REASONING

Cognitive load theory proposes three types of load; intrinsic, extraneous, and germane. The complexity of the problem and the expertise of the problem solver, or learner, are the main elements that make up intrinsic load. In clinical medicine, one cannot change the intrinsic nature of the problem presented or the expertise of the clinician at that time in that particular area; thus, the intrinsic load is fairly immutable in the short term. However, in instructional design, an educator may decide to present a simpler problem in order to reduce overall cognitive load.

The second type of cognitive load is extraneous load, which is increased by processes that are potentially irrelevant or superfluous and do not contribute to learning. This load is related to how the problem is presented, along with other things that may be distracting during a case presentation (pagers, other patient needs, lack of sleep). Commonly in case presentations, a lot of data is provided at once, and the challenge for the clinician is to prioritize and categorize the information. Our clinician has already prepared himself for this with the creation of his "buckets." This allows him to manage cognitive load and minimize extraneous load as the problem is presented.

The final type of cognitive load is germane load. This describes the working memory processes that are necessary for acquiring new knowledge, or expanding upon existing knowledge. The three types of load are additive, and as working memory is not unlimited, our clinician and his audience must manage the intrinsic and extraneous load in order to learn from this case. As the intrinsic load is difficult to change, clinicians primarily manage extraneous load by avoiding distractions, thus allowing optimum conditions within working memory. Similarly, in instructional design, the timing of concepts and format in which material is presented can optimize germane load.

At this time, our expert clinician has gathered more information about the syncope and about the patient himself. This information, particularly the recent gastrointestinal bleeding, seems to fit into the bucket for orthostatic hypotension. He has not forgotten about his other buckets, however, as he plans to focus on the cardiovascular and neurologic exams.

He also makes no attempt to place into context the significant weight loss, other past medical history, or medications. Our clinician has a well-developed schema for diagnosing syncope, and he is looking for specific details to sort into his "buckets." Those details that do not seem immediately relevant may be tabled, at least initially. This helps to manage his extraneous load, by initially focusing only on certain pieces of information provided. Of course, this is also a potential source of error, if the clinician does not return to all of the information presented, and place it into context with the physical exam findings. His schema will help prevent this, as he can return to each of the buckets to be sure that they have been adequately assessed to rule in or out the correct diagnosis.

CLINICAL INFORMATION

On physical exam, the patient's vital signs were heart rate of 92 bpm, blood pressure of 157/91 mmHg, respiratory rate of 18 rpm, and temperature of 97.5 °F. Orthostatic vital signs were normal. Cardiac auscultation revealed a regular rate and rhythm without murmurs or gallops. Detailed abdominal, pulmonary, vascular, skin, lymph node, and genitourinary exams were normal. His neurological exam revealed intact strength, normal gait, normal cranial nerves, and no sensory deficits. He had a normal Romberg test.

Laboratory data on admission were notable for a hematocrit of 24.6 %, hemoglobin of 7.8 g/dL, MCV of 90.6 fL, BUN of 27 mg/dL, creatinine of 1.9 mg/dL, glucose of 286 mg/dL, calcium of 9.1 mg/dL, total protein of 9.5 mg/dL, albumin of 2.8 mg/dL, and venous lactic acid of 5.2 mg/dL. Urinalysis demonstrated 2+ protein. The remainder of the patient's basic metabolic panel, urinalysis, and complete blood count were normal. An ECG was notable only for sinus tachycardia at 100 bpm.

A magnetic resonance imaging and angiogram of the brain and neck demonstrated no abnormalities. Similarly, a carotid Doppler and transthoracic echocardiogram were unremarkable.

CLINICIAN RESPONSE

There are several findings of interest from the initial laboratory evaluation, including renal insufficiency, proteinuria, anemia, an elevated lactic acid level, and elevated protein with hypoalbuminemia. I would be interested in obtaining information on his prior renal function, including prior urinalysis and (if previously performed) a measure of albumin in his urine. As is often the case, the imaging studies were not helpful; although the normal ECG and echocardiogram are somewhat reassuring. I would also suspect that this patient was on telemetry during the hospitalization, and significant arrhythmias would have been detected.

An interesting observation is that the gap between the total protein and the albumin is high. In a 70-year-old, one would need to consider multiple myeloma, which may or may not be related to the syncope. I would check serum protein electrophoresis (SPEP), serum immunofixation and free light chain assay to further evaluate the protein gap. If results suggest a monoclonal gammopathy, other valuable studies would include quantitative immunoglobulins, a bone survey, and a bone marrow aspiration and biopsy as well as a measure of serum viscosity.

CLINICAL REASONING

Now our clinician returns to the information presented earlier to place it into context with the physical exam and results of testing. His initial concern for orthostatic hypotension becomes less likely in the setting of normal vital signs. The next consideration, of a cardiogenic etiology for syncope, also becomes less likely with a normal exam and ECG. Rather than ignoring these pieces of data that conflict with his expectations, our expert broadens his differential diagnosis. He is careful to review all pieces of data, even those that may not initially seem relevant.

Here, we see the clinician return to his initial schema of large "buckets" in order to be sure that a broad differential diagnosis is considered. He reframes the long list of laboratory values and test results into potential diagnoses, which he can then sort into each of these buckets as a test for which might hold the final diagnosis. He notes the renal insufficiency, elevated lactic acid, and the protein gap. He focuses particularly on the protein gap in the setting of anemia and renal dysfunction, which highlights the potential for myeloma. Lactic acidosis without evidence of hypoperfusion could suggest malignancy. He is not yet sure how to tie this to the presenting complaint, but is sure to pursue further evaluation and look for more information.

CLINICAL INFORMATION

Further work-up of the globulin gap was undertaken. An SPEP demonstrated the presence of an IgM kappa monoclonal band, with IgM level at 7030 mg/dL.

CLINICIAN RESPONSE

This information definitely helps. Waldenström's macroglobulinemia is associated with a high IgM level. IgM is a pentamer and is much more likely to cause symptoms related to hyperviscosity, compared with an elevated IgG of the same level. This patient has a fairly large IgM spike. Elevation of IgM levels leads to an increase in serum viscosity, which can cause neurologic symptoms, often involving the posterior circulation, including vertigo, hearing loss, blurred or double vision, and ataxia. Other, more generalized neurologic symptoms, such as headache, alterations in consciousness, and seizures, can occur. Less frequently, hyperviscosity can result in syncope or stroke. These neurologic symptoms of Waldenström's would fall into a new "bucket" for syncope as these symptoms are not caused by the cardiovascular system, neural reflexes, or orthostasis. Instead, slow vascular flow and anemia contribute to global cerebral hypoperfusion. We might call this the "other" bucket, which could also could hold diagnoses like polycythemia vera or cryoglobulinemia.

In addition, gastrointestinal bleeding, as seen in this patient, can be caused by elevated M protein, presumably related to hyperviscosity in intestinal/colonic small vessels with associated bleeding or with amyloid infiltration into the intestinal or colonic wall.

Hyperviscosity is a clinical diagnosis, and treatment should be started without waiting on a test result. However, the diagnosis is confirmed by measuring serum viscosity. Viscosity is measured in centipoises, with water being 1.0 and normal serum being 1.4–1.8 centipoises. My hypothesis is that this patient had a markedly elevated serum viscosity.

CLINICAL REASONING

Our clinician utilized the creation of chunks or "buckets" of potential diagnoses that he could consider in turn, so as to more efficiently process the information as it was delivered, allowing him to focus on the pertinent clinical information. This allowed him to remain facile enough to consider the protein gap, even though it did not seem immediately related to the syncope. By following that evaluation to its conclusion, our expert clinician found a potential diagnosis. Had he been overwhelmed by excess cognitive load, he may have elected to defer evaluation to a later setting. Instead, as the results returned, he compared the data that he had to potential etiologies, and uncovered a rare diagnosis with overlap between the two.

Hyperviscosity as an etiology of syncope was not previously considered by our clinician, but now can be added into his schema, in a new "other" bucket, which also reminds him of other unusual causes of syncope. Similarly, the learners in our audience now have a new schema for thinking about syncope, which can be applied to other cases. As new diagnoses for syncope are taught, the learners can determine into which bucket they might fit, or add new buckets as our clinician did. The cognitive load needed for germane load in this situation is only available to learners if the intrinsic and extraneous loads are sufficiently managed.

CLINICAL INFORMATION

The patient's bone marrow biopsy was consistent with lymphoplasmacytic lymphoma. Serum viscosity was measured at 8.9 centipoises. Given the clinical manifestations, bone marrow biopsy, and cytogenetics analysis, the diagnosis of Waldenström's macroglobulinemia was made. The patient was started on plasmapheresis before beginning chemotherapy with cyclophosphamide, bortezomib, and dexamethasone. At 6-month follow-up, his symptoms were improved, and he had not experienced further syncope or near syncope.

DISCUSSION

This case highlights cognitive load theory, as it can be applied to clinical medicine. Cognitive load theory discusses how working memory is strained by a particular problem, and outlines three types of load: intrinsic, extraneous, and germane.[3] Intrinsic load relates to the nature of the problem and the expertise of the problem solver. Extraneous load relates to how the problem is presented and increases with distractions from potentially irrelevant information; the vast amount of laboratory data in the case is an example. Finally, germane load is the necessary working memory power that is required for learning. These types of cognitive load may be considered to be additive, and each learner has a maximum amount of cognitive load possible that will still give room for the work required for learning, or germane load, to occur. To give a different clinical example, a woman with recurrent urinary tract infections who now presents with fever and dysuria represents a case with low intrinsic load, as the diagnosis is not particularly challenging when the patient returns with the same problem they had before. If the presentation was clouded with a variety of extra details in history or physical exam, or if it presented in the midst of a busy clinic day, that would increase the extraneous load. However, when the problem is more complex, or the problem solver has less expertise in an area, the intrinsic load increases, and the clinician must find a way to reduce extraneous load so that learning can occur.

In this case of syncope, intrinsic cognitive load is high, as the case is complex. The discussant minimizes extraneous load by starting with a schema that he has previously utilized, placing differential diagnoses inside larger "buckets" of cardiogenic, neurally mediated, or orthostatic diagnoses. He can then easily "chunk" several pieces of information together, allowing his working memory to treat each chunk as a single piece. He can return to his larger schema throughout the case to be sure that he has not forgotten a potential diagnosis or ignored a piece of data.

This schema also helps to focus his germane load, as he has a clear system for thinking about new diagnoses related to syncope, and he can further refine his approach as he learns more and faces more cases with new diagnoses. By adequately managing the extraneous load in this case, he has the power within working memory to learn.

CLINICAL TEACHING POINTS

1. Syncope is a common complaint with a broad differential diagnosis. One framework for working through this diagnosis is to group potential diagnoses into categories of neurally mediated, cardiovascular, orthostatic, or other rarer etiologies.
2. Waldenstrom's Macroglobulinema (WM) is an infrequently occurring B cell lymphoma. It is a lymphoplasmacytic leukemia, in which there is an overproduction of IgM.[4,5] Patients with WM may have neurologic manifestations either from hyperviscosity or related to direct infiltration of lymphoplasmacytic cells into the CSF; the latter manifestations are known as the Bing Neel syndrome.[6] Neurologic manifestations include visual and auditory disturbances, headache, confusion, dizziness, vertigo, and rarely syncope or stroke.
3. Serum viscosity is measured by comparing the patient's serum viscosity with that of water. The result is expressed in centipoises. About one-third of patients with WM will have serum viscosity over four centipoises. Almost all patients will be symptomatic at or above a level of eight centipoises.[6]
4. Hyperviscosity due to WM is treated with plasmapheresis to remove IgM protein, followed by chemotherapy to treat the underlying malignancy. Hyperviscosity should be treated when patients have symptoms attributable to hyperviscosity, not purely based on a particular viscosity result.[7]

Contributor: *Dr. Yvette Cua-Ramirez for providing the video of the live session. Dr. Bob Means for insight into the Bing Neel syndrome and neurologic sequlae of hyperviscosity.*

Corresponding Author: *Erin D. Snyder, M.D.; University of Alabama at Birmingham, Birmingham, AL, USA (e-mail: esnyder@uab.edu).*

Compliance with Ethical Standards:

Prior Presentations: *The case presented here was presented as a Clinical Vignette Unknown at the Southern Society of General Internal*

Medicine, New Orleans, February 20–22, 2014. The clinical information and case discussion closely reflect the topics discussed. The case description was modified slightly for instructional purposes.

Conflicts of Interest: *The authors declare that they do not have a conflict of interest.*

Disclosures: *The opinions expressed in this article are those of the authors alone and do not reflect the views of the Department of Veterans Affairs.*

REFERENCES

1. **Durning SJ, Artino AR Jr, Schuwirth L, van der Vleuten C.** Clarifying assumptions to enhance our understanding and assessment of clinical reasoning. Acad Med. 2013;88:442–8.
2. **Sweller J, van Merriënboer JJG, Paas FGWC.** Cognitive architecture and instructional design. Educ Psychol Rev. 1998;10:251–96.
3. **van Merriënboer JJG, Sweller J.** Cognitive load theory in health professional education: design principles and strategies. Med Educ. 2010;44:85–93.
4. **Vitolo U, Ferreri AJ, Montoto S.** Lymphoplasmacytic lymphoma-Waldenstrom's macroglobulinemia. Crit Rev Oncol Hematol. 2008;67:172–85.
5. **Ansell SM, Kyle RA, Reeder CB, et al.** Diagnosis and management of Waldenström macroglobulinemia: mayo stratification of macroglobulinemia and risk-adapted therapy (mSMART) guidelines. Mayo Clin Proc. 2010;85:824–33.
6. **Drouet T, Behin A, Psimaras D, Choquet S, Guillevin R, Hoang XK.** Bing-Neel syndrome revealing Waldenström's macroglobulinemia. Rev Neurol (Paris). 2010;166:66–75.
7. **Stone MJ, Bogen SA.** Evidence-based focused review of management of hyperviscosity syndrome. Blood. 2012;119:2205–8.