



Editorial in Response To “Case Report: Chronic Acalculous Cholecystitis Preceded by Coxsackievirus B4 Infection” [1]

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In response to the recently published article “Case report: chronic acalculous cholecystitis preceded by Coxsackievirus B4 infection” [1], the senior author postulates that the convergence of bias in medical care and atypical clinical presentations contributed to delayed diagnosis of acalculous cholecystitis. Upon first assessment of the basic case features, the initial diagnosis seemed self-evident. A 43-year-old Caucasian female with body mass index of 32.96 kg/m² presented to a suburban emergency room with complaints of epigastric pain. Vital signs were within normal limits. Imaging ultrasound imaging of upper abdomen was unremarkable. Given the estimated prevalence of 1 in 3 adults for obesity and gastro-esophageal reflux disease GERD [2,3], the physician's assistant discharged the woman with a prescription of an anti-acid and acetaminophen to address symptoms of GERD. She was taking 40mg daily omeprazole, adhered to a strict BRAT diet (banana, rice, applesauce, toast) and had lost 9kg since pain onset. The patient reported that the pain in the upper abdomen had progressively intensified over a 2-month time period and described the pain intensity level 9 out of 10 with severe radiating in the left-side frontal and posterior torso *aka* “Devil's Grip”. However, the superficial diagnosis disregarded that life-style modifications that failed to alleviate GERD-associated symptoms and the severity of the chest pain warranted further investigation. Did underlying biases play a role of prolonging the diagnosis of Coxsackievirus B4 infection, potentially contributing to the development of acalculous cholecystitis in this patient?

Cognitive bias, including self-aware explicit bias or underlying implicit bias of which the person is unaware, is pervasive in medicine and has implications for misdiagnoses

[4] and health disparities [5]. A Medscape Lifestyle survey of 15,800 physicians practicing in USA found that a staggering 62% of emergency room physicians self-report explicit bias towards patients [7]. Studies focused on gender bias in healthcare has consistently implicated poor medical response to women in acute pain [7] or chronic pain [8], as compared to male patients with identical symptoms, further exacerbated if the patient is of non-Caucasian ethnicity [9]. Although the patient consistently demonstrated healthy parameters for blood pressure, low cholesterol and low HbA1c, the focus of treatment plan was limited only to weight management. Was the patient dismissed for further investigation of the origin of pain due to anti-fat bias [10, 11]? Findings in the Medscape Lifestyle 2016 demonstrated that both male and female physicians 62%, (48% respectively) self-report explicit bias triggered by patients weight [6], which is consistent with evidence that implicit anti-fat bias is neurologically embedded [12]. An international panel of physicians recently published *Joint international consensus statement for ending stigma of obesity* in Nature Medicine, highlighting that bias against a patient due to weight can have multi-level consequences including health care barriers [13]. Lastly, there are implications for affinity bias creating a barrier for thorough work up for the patient of the case report. Affinity bias, which is a short-cut diagnoses strictly based on the most common presentations, is best summarized with the commonly used phrase, “Looks like a duck, quacks like a duck, must be a duck” [4]. Epigastric pain in obese middle-aged woman yields a putative diagnosis of GERD with no further investigation necessary. Yet the pain persisted.

Rare diseases with atypical presentations pose an inherent challenge to physicians with limited time interaction with patients. Regardless of the underlying cognitive bias that were relevant to the initial interaction of the patient and

physician's assistant in the emergency room, the diagnosis and treatment recommendations for GERD were insufficient to address the root of the chronic abdominal pain [14]. Pleurodynia triggered by infection with Coxsackievirus B4 is a rare clinical presentation in modern times, indirectly indicated by the significant drop of case and Pubmed searches after 1977 [15], thus practicing physicians who were born earlier than the Baby Boomer generation would likely have never encountered a case outside of medical text books. Pancreatic enzyme insufficiency associated with Coxsackievirus infection yet without underlying conditions of diabetes, cancer, autoimmunity or obstruction fails to fall within the parameters of the Tigar-O Classification System [16]. Furthermore, true incidence of chronic acalculous cholecystitis is unknown and considerably less common than acute acalculous cholecystitis with an estimated representation of 5-10% cases of acute cholecystitis [17]. Given the atypical combination of symptomatology described in the report case, the intensity, pattern of onset and anatomical distribution of the pain, primarily the characteristic Murphy's sign of intense pain provocation by applied pressure corresponding to anatomical location of the gall bladder, proved the key feature of the clinical presentation to yield the subsequent diagnostic work-up and recommendation for surgical intervention of cholecystectomy [18].

The involvement of pleural chest pain and left upper quadrant abdomen, regionally consistent with pancreatic inflammation, yield consideration of pleurodynia and pancreatitis as differential diagnosis, thus prompted work up for serological markers for Coxsackieviruses [19]. The intensity of the left abdominal quadrant and chest subsided, yet the right upper quadrant pain persisted for months with aggravated attacks triggered ingestion of saturated fats. Although the ultrasound and CT-scan imaging studies for the patient in the case study were unremarkable for gall bladder abnormalities, the injection of cholecystokinin (CCK) during the hepato-imino-diacetic acid (HIDA) scan simulated a symptomatic attack, similar to consumption of saturated fat. The CCK-induced provocation of symptoms proved to be a greater predictor of chronic acalculous cholecystitis than ultrasound or HIDA-scan ejection fraction [20]. In absence of any other definitive diagnostic findings after 10 months of symptoms, the gastroenterologist provided the patient with the surgical referral based on the classic Murphy sign, further evidence that pain presentation can be a key diagnostic parameter and should not be disregarded.

In context of the global COVID-19 pandemic, the challenges of overcoming cognitive biases to explore unusual differential diagnoses with an atypical presentation have broader implications beyond this individual case report. Accumulating cases reports [21, 22] linking SARS-CoV2 infection to acute acalculous cholecystitis prompted a statement on updated recommendations for laparoscopic cholecystectomy by World Society of Emergency Surgery [23]. Taking into account the diversity of clinical

presentations associated with disseminated SARS-CoV2, the possibility of patient developing viral-induced chronic acalculous cholecystitis is highly likely. The duration of pain and disease outcomes will be greatly influenced by the cognitive biases of the physician and their ability to assess a case that has not yet been included in the medical textbooks. To mitigate delayed diagnosis, physicians can overcome biases by listening to the patient, especially details of onset, anatomical distribution, and intensity of pain. I genuinely hope for timely surgical intervention to alleviate the pain for patients with acalculous cholecystitis. Given that I was the patient in the case report, I empathize with the challenge of enduring chronic pain and experiencing dismissive bias while navigating an imperfect healthcare system.

Statement of Ethics

Ethical Review

The senior author of the editorial and case study attests that the manuscript is an original writing contribution, free of evident plagiarism. The subject case report was compliant with ethical practices established by Nuremburg Code. A written informed consent was submitted by the subject patient and the project was approved by Internal Review Board at St. George's University in Grenada.

Conflict of Interest

The senior author of the editorial and case study has no conflicting established partnerships of financial or non-financial support and holds a primary academic role at St. George's University, West Indies. The senior author, Jane Harrington, is the subject patient and has a personal interest in promotion of the case study.

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