CLINICAL VIGNETTE

The *Girl* Who Cried Wolf

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A 38-year-old woman with type 2 insulin-dependent diabetes mellitus presented to the emergency department with abdominal pain, nausea, and vomiting. Her significant past medical history dated back to 2009 when she developed perforated sigmoid diverticulitis requiring a partial colectomy and colostomy with Hartman's pouch. She developed post-operative intra-abdominal abscesses requiring surgical drainage and lysis of adhesions and removal of the right ovary. The pathology of the ovary was reported as benign. After recovery, she had a takedown of the colostomy in 2010. This procedure was accompanied by a left ovarian cystectomy with salpingectomy, with pathological showing endometriosis. Subsequently, she presented to the emergency room with abdominal pain on several occasions and in 2012, she received another surgical intervention with lysis of adhesions and did well for a few years. She then moved to California and was first admitted to our facility in September 2015 for abdominal pain. In 2016, after several admissions for recurrent abdominal pain, she received another surgical intervention for lysis of adhesions. CT scan of the abdomen and pelvis did not show any acute pathology. She continued to have several emergency room visits for abdominal pain with nausea, vomiting, inability to tolerate oral intake, not related to her menstruation and most leading to hospitalizations. She always requested parenteral opioids for her abdominal pain due to vomiting during her emergency room and inpatient stay. Diabetic gastroparesis was ruled out by her gastroenterologist after outpatient testing. Once hospitalized, she would improve in a few days and would go home. She was believed to have cyclic vomiting syndrome. She admitted to frequently smoking marijuana at home to control her nausea. Over the years, she received numerous abdominal imaging scans without significant findings. Due to recurring presentation for the same chronic problem, the emergency room physician on this occasion only performed a plain abdominal x-ray which was reported insignificant. Her initial vital signs were blood pressure of 166/98 mmHg, heart rate 59 per minute, respiratory rate 22 breaths per minute, pulse oximetry of 100% at room air and body temperature of 98.9ºF. This was her 50th admission to our facility following her 59th emergency room visit in about three and half years. Our evaluation at admission, found abdominal tenderness and leukocytosis and we requested a CT scan of the abdomen and pelvis. It revealed a new finding of bilateral adrenal gland enlargement with periadrenal fat stranding suggesting either adrenal hemorrhage or adrenal congestion which can precede hemorrhage [Figure 1]. The latter was more plausible diagnosis and a.m. cortisol of 46 mcg/dL and ACTH 28 pg/mL, ruled out adrenal insufficiency.

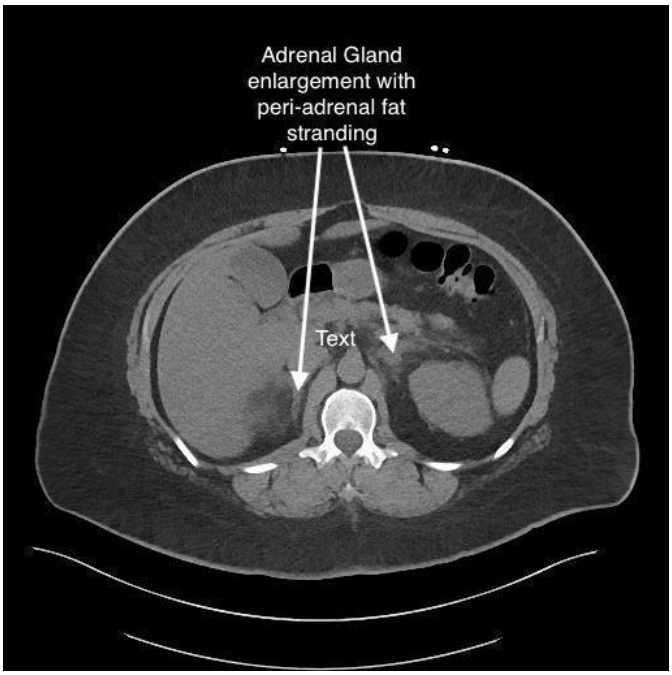

Figure 1.

Discussion

According to the CDC, about 11.5% of adults experience daily pain. In 2016 alone, an estimated 12,525,000 visits to the U.S. emergency department (ED) were attributed to abdominal pain and 2,769,000 visits for vomiting. The ED physicians face considerable challenge in identifying patients with objective explanation for pain versus others with opioid seeking behavior.[1-3] The dilemma is further complicated when the patients have significant past abdominal pathology leading to repeated imaging studies. With recurrent visits for the same complaint, raises questions about repeat CT imaging especially in women of child bearing age. None of the prior CT scans of the abdomen and pelvis revealed significant acute pathology until this admission.

Our patient was previously diagnosed with Cyclic Vomiting Syndrome (CVS) characterized by (i) stereotypical episodes of acute onset of vomiting lasting < 1 week; (ii) 3 or more episodes in prior year and 2 episodes in the last 6 months, occurring at least 1 week apart; (iii) absence of vomiting between episodes although milder symptoms can be present; and (iv) symptoms present for the last 3 months with onset 6 or more months prior.

The syndrome has a bimodal peak, at 5 years of age and at age 37. Physical and psychological stressors may be precipitants. Several etiologies have been proposed including mitochondrial DNA mutations and polymorphisms involving the cannabinoid receptor type1 and mu-opioid receptor genes, a dysfunctional hypothalamic-pituitary-adrenal axis or endocannabinoid system and autonomic nervous system dysfunction. This syndrome shares similarities with migraine headaches, both sharing similar pathophysiology and common therapeutic agents. Severe abdominal pain is present in 58-71% of adults suffering from CVS. Gastroparesis has chronic post prandial symptoms whereas, CVS symptoms are more episodic. Abortive therapy with nasal or subcutaneous triptan is recommended when initiated in the prodromal phase. Rescue therapy after symptoms develop includes intravenous fluids, parenteral ondansetron and judicious use of opioids when abdominal pain is present.[4] We believe our patient was suffering from Cannabinoid Hyperemesis Syndrome, (CHS) a subset of CVS. Cannabis is used for its anti-emetic properties. There are 2 types of cannabinoid receptors: CB1 in the central, peripheral, and enteric nervous systems, which promotes the anti-nausea effect and CB2 in the lymphatic system of terminal ileum. Overstimulation of CB1 receptors in the enteric plexus by tetrahydrocannabinol, cannabis's active component, can exceed the individual's threshold is believed to the mechanism for Cannabinoid hyperemesis syndrome. The syndrome has been associated with leukocytosis, which was present in our patient. Symptoms do not respond to conventional antiemetics however, hot water baths provide relief. Stopping cannabis is the best treatment.[4,5]

The CT scan finding of bilateral adrenal gland congestion was unexpected. Her clinical presentation with vomiting, feeling of listlessness, abdominal tenderness and leukocytosis was concerning. Adrenal glands are supplied by three arterial sources and have a single venous drainage. During periods of physiological stress, there is endothelial damage and risk of venous drainage thrombosis leading to congestion followed by hemorrhage. Post-operative state, sepsis, hypercoagulable states, heparin use are some of the risk factors [see Table 1]. In our patient, the major source of stress was the manifestation of CHS. Further research is needed to determine if CHS can be a risk factor for developing adrenal congestion. Adrenal congestion is considered a precursor of adrenal hemorrhage, which can lead to acute adrenal insufficiency when greater than ninety percent of both adrenal glands' cortices are compromised.[6] Steroid supplementation is generally initiated empirically. Our endocrinologist advised us against empiric steroid treatment given normal baseline a.m. cortisol and ACTH values, overall hemodynamic stability and gradual resolving distress from her symptoms of CHS. After discharges in search of new healthcare providers, she changed her health insurance. In addition to primary care, endocrinology follow-up was arranged with her new providers.

Our case of the *girl* who cried wolf brings up several important learning issues in modern day healthcare. First, the problem of overutilization of the ED, hospitalizations for chronic recurrent pain/vomiting and the chronic use for parenteral opioids. We have previously reported the risk of missing important medical pathology when patients present encephalopathic with opioid overdose.[7] Fortunately, our patient never presented with opioid overdose. Coordination with primary physicians involved in her care during different admissions, resulted in a single pain medicine specialist who followed the patient and prescribed the analgesic regimen on all her admissions. The Controlled Substance Utilization Review and Evaluation System (CURES) database helped us understand her outpatient opioid prescriptions. A second learning issue involves, the increasing risk of hyperemesis cannabinoid syndrome with legalization of medical marijuana and the patient's refusal to stop marijuana use as treatment for CHS. Lastly, the conundrum for the treating physicians on how much evaluation is needed for a very similar recurring presentations, which was confounded by adrenal congestion on CT scan, despite no signs of active adrenal insufficiency.

Table 1.

Causes of Non-Traumatic Adrenal Hemorrhage	**Examples of Clinical Conditions to consider in**
Physiologic Stress	Recent Surgery Hypotension Sepsis Burns
Coagulopathy and Thrombocytopenia leading to intraglandular bleeding	Anticoagulant use
Hypercoagulable States leading to adrenal vein thrombus	Antiphospholipid Syndromes

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