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Mycotoxin-Triggered Attacks of Nausea, Vomiting, and Abdominal Pain and Episodes of Pseudo-Obstruction

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Abstract

Determining the etiology of episodic abdominal pain, nausea and vomiting with and without pseudo-obstruction and implementing effective treatment can be challenging. Mycotoxins activate mast cells which rapidly degranulate releasing pro-inflammatory cytokines. Mast cells commonly reside in the gastrointestinal mucosa and adjacent to nerves. Aberrant mast cells with loss of control due to genetic abnormalities are present in mast cell activation syndrome, a common, yet often unrecognized multisystemic disorder. Mold exposure with consequent toxicity by its mycotoxins can present with complex multisystem disorders along with abdominal pain, nausea, and vomiting. A 63-year-old man presented with episodic attacks of abdominal pain, nausea and vomiting when he was exposed to dwellings with mold. Over a 4-year period he was admitted and there was radiographic evidence of dilation of the stomach and small intestine during three admissions and dilation of the colon in the other admission. When the patient was subsequently diagnosed and treated for underlying mast cell activation syndrome, the attacks ceased, and he has been healthy for the last three years. Recognition that mycotoxins can act as triggering factors is essential to effectively treat patients with and without mast cell activation syndrome who have these gastrointestinal attacks and episodic gastrointestinal pseudo-obstruction.

Keywords: Abdominal Pain, Gastroparesis, Ileus, Mast Cell, Mast Cell Activation Syndrome, Mold, Mycotoxins, Nausea, Pseudo-Obstruction, Vomiting

INTRODUCTION

Attacks of abdominal pain, nausea and vomiting may be difficult to diagnose and treat [1]. Quality of life is poor and economic impact is often significant for those afflicted with nausea [2]. Treating and determining the etiology of intestinal pseudo-obstruction is often difficult [3]. Indoor exposure to molds and mycotoxins is generally unrecognized as causes for nausea in both patients with and without mast cell activation syndrome (MCAS) [4-7]. The most common variant of mast cell activation disease (MCAD) is MCAS, and this presents with many inflammatory and allergic symptoms and systemic syndromes [8]. In Germany, the prevalence of MCAD was estimated to be 17% of the population [9]. Systemic mastocytosis (SM) is a well-known MCAD that is malignant and rare (incidence of 0.89 cases per 100,000 persons per year) [10]. The prevalence of nausea in a case series of 413 MCAS patients was 57% [5]. The prevalence of nausea in a case series of 83 SM patients was 23% [11].

Indoor mold exposure can be associated with nausea [12-14]. Lieberman et al reported that 16/48 (33%) consecutive mold-affected patients had nausea [12]. Hyvonen et al

reported 24/47 (51%) students in a water damaged school had nausea as compared to 2/56 (4%) students in a control school (p<0.001) [15].

Mast cells are immune cells that are present in most tissues that surround blood vessels and nerves, and are found in the skin, lung mucosa, and digestive tract, as well as in the oral cavity, nose, and conjunctiva [16]. Mold contamination in buildings is quite common [17-19]. Molds produce numerous secondary metabolites known as mycotoxins [20]. Exposure to mycotoxins has been linked to activation of mast cells, and IgE antibodies to mycotoxins stimulate mast cells to release heparin, histamine, pro-inflammatory cytokines, and prostaglandin D2 [21,22]. Signs of this release include neurological symptoms such as brain fog, headaches, nausea, fatigue, and irritation of the respiratory tract [23-25]. Recent publications show that this stimulation by IgE antibodies to mycotoxins in serum can lead to Mast Cell Activation

A wide variety of infections and toxic exposures are triggers for activation of MCAS [18-24]. Mycotoxins can be absorbed via nasal mucosa, lungs, gastrointestinal track and skin and readily pass the blood-brain barrier [26-31]. Molds release

mycotoxins which activate normal mast cells (MCs) [25] as well as unregulated MCs in MCAS (authors personal observations). Indoor mold exposure has been linked to MC degranulation, secretion of cytokines and chemokines, neutrophil recruitment, and increased intestinal permeability [32-34].

CASE REPORT

A 63-year-old Caucasian male property manager presented with a 4-year history of frequent attacks of nausea, vomiting and abdominal pain. These attacks occurred during work when he inspected houses that had water damage (Figure 1). He had four hospitalizations for the most severe of his numerous attacks and each showed an abnormal

computerized tomography (CT) scan. In January 2016, there were dilated loops of small intestine and fluid in a distended stomach. In September 2016, the large intestine was dilated with gas and fluid. In August 2018, the jejunum and proximal to mid ileum were dilated (Figure 2) and he underwent exploratory surgery. The operative report described dilated loops of small intestine without evidence of a transition point or adhesions. Finally in January 2020, he had a small bowel ileus which required prolonged nasal gastric tube decompression. After 8 days, a diatrizoate meglumine and diatrizoate sodium solution study via a nasogastric tube demonstrated dilated small bowel loops and a 5-hour transit time to the cecum.



Figure 1. Moldy ceiling in one of the houses that the patient inspected.

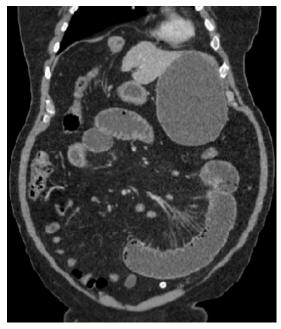


Figure 2. Computerized tomography (CT) image after 4 days of pain, vomiting and diarrhea with first emergency room evaluation. CT demonstrated a fluid-filled, enlarged stomach and mildly dilated and fluid-filled loops of the mid and proximal small intestine.

After discharge he sought a second opinion. A detailed review of medical records including the operative report, review of systems, childhood and teenage medical history, and family history was performed. The mast cell mediator release syndrome (MCMRS) questionnaire (Appendix A) symptom score was 15 in six of ten systems ("diagnostic criteria of a mast cell mediator release syndrome are clinically confirmed") [9].. His most severe symptoms included gastrointestinal symptoms, chronic fatigue, headaches, episodic chest pain, and dyspnea. Mild tinnitus was present for 10 years. He also had near fainting spells when working in moldy homes. His parents and siblings did not have undiagnosed medical syndromes or symptoms. His daughter has hypermobile Ehlers-Danlos syndrome and autonomic dysfunction with orthostatic intolerance. Physical examination showed that he was short of breath moving from the chair to the examining table. His lungs were clear to auscultation. The chest radiograph was normal. The abdomen exam was normal. A partial MCAS work up that measured four blood mediator tests revealed an elevated histamine level (3.9 ng/mL; normal ≤1.8). Urine mediator testing was not performed.

The patient has had significant improvements in all chronic symptoms with MC-directed therapy: histamine-1 and histamine-2 receptor antagonists, vitamins C and D, and low dose naltrexone [35,36]. He had no further GI attacks unless he went into a particularly severely moldy house without wearing a mask. He subsequently changed jobs and had no symptoms. In 2024 he had a brief admission for similar symptoms that occurred when he tried to remove moldy drywall from his own garage.

DISCUSSION

Nausea and vomiting are common problems in MCAS patients and can have a significant impact on quality of life as demonstrated in this report. Activation of MCs by a variety of infections (bacteria, rickettsia, fungi, parasites, and viruses) occurs by direct and indirect mechanisms [33,37]. The role of mold and mycotoxin in MCAS is not well known in general medicine. Mold and mycotoxins activate normal MCs which lead to pro-inflammatory cytokines such as prostaglandin D2, histamine, and antibody production [32,33,38,39]. Stimulation of dysregulated, mutated MCs in MCAS patients activates normal MCs which further amplifies the effect.

Exposure to molds and mycotoxins can present with a multisystemic illness in people without other diseases [40]. The commonly accepted presentation of mold toxicity is limited to asthma and sinusitis, but lately it has been expanded to include a wide array of multisystemic symptoms [12,40]. Nausea has been noted as a complaint in approximately 15% of 1,000 patients who were positive for mycotoxin antibodies (Andrew W. Campbell, M.D., personal observations). Autoimmune antibody response to molds and mycotoxins with subsequent demyelination and autoimmune nerve degeneration has been demonstrated [41,42]. One report

linked two cases of new-onset chronic inflammatory demyelinating polyneuropathy (CIDP) to heavy indoor mold exposure [42]. Theoretically this could be caused by central or peripheral nervous system inflammation. To explain nausea, demyelination of the vagal nerve or enteric nervous system could lead to subsequent abnormal gastrointestinal motility. Alternatively, central nervous system inflammation in various areas of the brain could lead to nausea. Proinflammatory cytokines have been demonstrated in various brain regions in response to mycotoxins in a mouse model [43]. Theoretically, release of mediators by mast cells adjacent to gastrointestinal parasympathetic nerves could lead to spontaneous ileus. Spontaneous bloating is common in MCAS [6].

This case reports illustrates the severe impact of mold exposure and mycotoxins in a patient with previously undiagnosed MCAS. There was radiographic and surgical evidence of gastroparesis, small intestinal pseudo-obstruction, and colonic pseudo-obstruction. His acute attacks improved by having the patient wear a mask during his work and taking MC-directed medical therapy. Ultimately, he changed to a different job and remained healthy.

There are inherent problems in the diagnosis and treatment of mold-related diseases. There are no studies comparing immunoglobulin testing versus urine tests. There are no double-blind, placebo-controlled treatment studies. The benefit of using immunoglobulin testing is the specificity of the immune response [44]. A study by Vojdani et al reported that levels of antibodies to Penicillium notatum, Aspergillus niger, Stachybotrys chartarum, and Satratoxin-H were significantly higher in 500 patients exposed to high levels of mold as compared to 500 unexposed controls (P<0.001 for all 4 comparisons) [44].

Nausea can be a serious consequence of mold and mycotoxin exposure. MC activation by mycotoxins is a driver of inflammation [38]. Worsening of MCAS by mycotoxins has been observed by practitioners, but not reported in the literature to our knowledge. More studies are needed to determine the relationships between mold, mycotoxins, and their effects on MCs and MCAS.

This case is remarkable for the severe and lengthy clinical presentation with supporting radiographic evidence. The climate crisis is responsible for increasingly causing flooding of homes and business places which increases the risk of heavy mold exposure [45]. The impact of mycotoxins in the development of gastrointestinal and systemic disorders is not well appreciated among physicians and other medical professionals. Gastrointestinal symptoms may be the primary presentation of mycotoxin diseases.

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APPENDIX 1.

MAST CELL MEDIATOR RELEASE SYNDROME QUESTIONNAI	RE
Name: Birth date: Date: _	
Answer all of the following symptoms/questions, even if the not necessarily present currently but in the past), or may seen	y are only slightly bothersome, rarely occurring (for instance, m not be related to your main problems.
Do you get colds regularly which then turn into bacterial nf Yes No	rections such as bronchitis or sinus infections?
Has the course of your illness been episodic (and/or with atta	acks)?Yes No
Have the symptom-free periods become shorter and shorter?	Yes No
* * * * * * * * * * * * * * * * * * * *	er the intensity level on the line next to the box. The number d. If the statement does not apply, do not check the box or enter
Use the range of 1 (very mild)to 10 (unbearable) to reflect the	e level of your discomfort. Example: 🗸 6
The following symptoms occur repeatedly or may be cons	stant:
GENERAL HEALTH	Applies Intensity
Significant physicalweakness or fatigue doing everyday activi	ties. ———
Extreme fatigue attacks, it can be hard to keep eyes open	
At times I lose weight despite maintaining my normal diet	
EYES, EARS, NOSE, MOUTH	
Ears have ringing or odd sounds	
Eyesare dry, itchy,red,burning, or feel gritty	
Runny or stuffy nose	
Inflammation or ulcers of the mouth	<u> </u>
Score 1 fo	or any of the 4 symptoms
CHEST and HEART	
Burning and/or pressure pain in the chest	
(Normal electrocardiogram or stress test; or not severe enoug	gh to go to ER)
Rapid heart rate (rapid palpitations)	
Redness or flushing of the skin, especially face or upper body	
	Score 2 if positive
Hot flashes (usually with dry skin lasting 2 to 5 minutes, rare	ly 10minutes and often occur with nausea or other symptoms.
(these are not menopausal hot flashes with wet sweats)	Score 2 if positive
Sudden dizziness/lightheadedness withfainting or near faint.	
	Score 2 if positive
LUNGS	
Irritable dry cough or need to cough	
Feeling of shortness of breath or difficulty taking a full breath	······
Asthma-like complaints (wheezing)	
Score 1 if	one or more is present

ABDOMEN			
Attacks of visible bloating or distension within minutes			-
Pain in the abdomen			-
Pain is burning			-
Pain is crampy or spastic			-
Pain is associated with diarrhea (watery or loose stool)			-
Nausea (with or without vomiting)			-
Do antihistamines help reduce nausea (examples: Allegra, cetirizine,			
Claritin, diphenhydramine, Xyzal, Zyrtec, etc.)?Yes No_			
(this does not include nausea relief from Zofran or Ondansetron)			
URINE/PELVIS			
Bladderand/or pelvicpain (this applies to women and men) and is often urination and may be associated with pain during sex	en associa	ated withp	ainful, frequent and/or urgent
(during these times bacterial cultures and urine analysis are normal)			
NEUROLOGIC and MUSCULOSKELETAL			
Migraine-like headaches (throbbing on one side only or have			
been diagnosed as a migraine – (these are NOT tension headaches)			-
Brain fog – word finding problems and/or concentration			
difficulties with or without associated insomnia episodes			-
Leg or arm pain and/or altered feelings including			
numbness, tingling, burning, sharp pain, and pins and needles			-
(this does not respond to over-the-counter pain medicine)			
SKIN(see the Photographic Examples at end)			
Hives (red raised itchy spots)			-
Hemangiomas (raised or flat bright red spots)			-
During attacks there are itchy skin lesions that look like acne in the			
corners of thenasal-lip area, as well as, the chin and forehead			-
Knots or nodulesunder the skin			-
Painless, non-itchy swelling (especially lips, cheeks, eyelids)			-
Itching in area around the anus during attacks			
HEMATOLOGIC			
Bruising afterminor injuries			-
Unusual nose bleeds			-
Women only: significant menstrual bleeding			-
Score 1 if one or mo	re is pres	sent	
Are any of the symptoms or complaints listed above worsened by:			
High histamine foods (such as alcohol, cheese, chocolate,			
tuna, cured fish/meat, left-over meat, raisins, tomatoes,)			-
Sleep deprivation (awake for more than 24 hours)			-

Hunger or fasting (no food all day)	
BONE	
Bone pain that usuallyoccursin more than one bone	
Score 1 if pr	rocont
-	esent
Bone density test showed osteoporosis or osteopenia	
without a known cause	
and/or	
Whole-body nuclear scintigraphy showed areas of	
increased bone metabolism without a known cause	
Score 1 if one or more is pro	ncont
Score 1 it one of more is pro	:sent
	
Laboratory Data	
At least once during the disease phases there was:	
	Applies
Hyperbilirubinemia up to about 2.5 mg% with the exclusion of	
Meulengracht/Gilbert's syndrome or another hereditarydisorders	
Increase in transaminases:	
γGT and/or	
ALT and/or	
AST and/or	
Score 1 if one or more is present.	□1
AST increased >10 fold (subtract 1 point and look for other diseases)	□- 1
Hypercholesterolemia (patient must be normal or underweight)	□ 1
Low titer autoantibodies without a corresponding organ symptom	1
Mast cell mediators:	- 0
Tryptase in serum was normal	□ 0
Tryptasewas marginally increased Tryptaseingrouped > 2 times the upper limit	□3 □10
Tryptaseincreased >2 times the upper limit Histamine in plasma was normal	□ 10 □ 0
Histaminewas marginally increased	□ 3
Histamineincreased >2 times the upper limit	□ 3 □ 10
Prostaglandin D2 in plasma was normal	□ 1 0
Prostaglandin D2 was marginally increased	□ 3
Prostaglandin D2increased >2 times the upper limit	□ 10
Heparin and/or factor VIII in plasma was/were normal	□ 0
Heparin and/or factor VIII was/were elevated (and bleeding	
disorders were excluded).	□ 3
Chromogranin-A in serum was normal	0
Chromogranin-Awas increased (and other causes were excluded)	□ 3
Leukotriene E-4 in urine was normal	0
Leukotriene E-4was marginally increased	1
Leukotriene E-4was10 times the upper limit	5
Leukotriene E-4was >10 times the normal limit	10
N-methylhistamine in urine was normal	0
N-methylhistamine was marginally increased	1
N-methylhistamine was10 times the upper limit	□ 5
N-methylhistamine was >10 times the normal limit	10

2,3 dinor 11b PG F2 alpha in urine was normal	0	
2,3 dinor 11b PG F2 alpha was marginally increased	1	
2,3 dinor 11b PG F2 alpha was 10 times the upper limit	5	
2,3 dinor 11b PG F2 alpha was >10 times the normal limit	□ 10	
Other conspicuous laboratory findings (please name with values)	□ 0	
Procedures and Imaging		
Esophagogastroduodenoscopy or associated biopsies had:		
no pathological findings	0	
or		
mild inflammation	1	
or		
Helicobacter pylori-negative and NSAID-negative erosions		
and/or ulcers	□ 3	
or		
diffuse and/or focalmast cell infiltrates ≥20/hpf with rounded shape	□5	
or		
Mast cell nests and/or sheets of spindle-shaped mast cells		
and/or CD25-positive mast cells	□ 10	
Colonoscopy and associated biopsies had:		
no pathological findings	0	
or		
mild inflammation	1	
or		
focal and/or disseminated dense infiltrates of		
morphologically inconspicuous mast cells	□5	
or		
Mast cell nests and/or sheets of spindle-shaped mast cells		
and/or CD25-positive mast cells	10	
Enlargement of the spleen		
and/or enlargement of the liver		
and of emargement of the niver	□ □ 1	
	⊔ 1	

Diseases and disorders below should be excluded in order help confirm the presence of a mast cell disorder. Symptoms in some organ/tissue systems can be similar in both. Evaluate both checklists and the numerical values listed to the right of each box. Add together to get a sum. The data should be entered by the physician.

Sum 9 to 13 = pathological activation of mast cells as cause of complaint is assumed.

Sum ≥ 14 = diagnosis of mast cell mediator release syndromeisclinically confirmed.

Sum of points: ____Diagnosis: mast cell mediator release syndrome

5 or more systems involved may also be important.

Differential diagnosis and testing for disorders that are multi-systemic diseases, present with some similar symptoms, or exacerbate mast cell activation

Endocrine disorders - all are multi-sytemic

Adrenal insufficiency (cosyntrophin stimulation test)

Diabetes mellitus (history and labs – Type 1 or 2 with systemic complications)

Endometriosis (gynecologic exam, laparoscopy)

Fabry disease(neuropathic pain, fatigue, angiokeratomas, cloudy cornea, genetic test)

Porphyria (lab: spot PBG urine)

Thyroid disorders - multi-systemic and can exacerbate MCAS (labs: thyroid panel)

Gastrointestinal disorders

Amyloidosis - multi-systemic (fat biopsy, rectal biopsy)

Celiac disease - multi-systemic and can exacerbate MCAS (antibody studies, endoscopic biopsy)

Cholecystitis (ultrasound, DISIDA imaging)

Chronic bacterial infection or post-infectious autoimmune state (fecal PCR, lactulose breath test) – multi-systemic and may exacerbate MCAS (endoscopic biopsy, urea breath test, antibody study)

Hepatitis multi-systemic (hepatitis profile, other laboratory tests)

Inflammatory bowel disease – multi-systemic (colonoscopy/ileoscopy and biopsy; video capsule endoscopy)

Lactose, sucrose, or fructose intolerance as cause of bloating and altered bowel habits (history, specific breath tests)

Median arcuate ligament syndrome – multi-system and can exacerbate MCAS (auscultation, CT angiography with deep expiration views)

Microscopic colitis associated with celiac disease or cryptosporidiosis - multi-systemic (colonoscopy biopsy, cryptosporidiosis antigen)

Parasitic infection - multi-systemic (fecal antigen testing, ova and parasite exam, PCR testing)

Small bowel obstruction with and without small intestinal bacterial overgrowth – multi-systemic (adhesions, volvulus, hernia, tumors) (history, physical, imaging studies, lactulose breath testing)

Small intestinal bacterial overgrowth – multi-systemic and exacerbates MCAS (lactulose breath test, glucose breath test, duodenal or jejunal aspirate culture)

Immunological, Inflammatory and Rheumatologic diseases- all multi-systemic

Anti-phospholipid syndrome (history, antibody tests)

Asthma and atopic diseases including chronic urticaria (history, allergy testing – skin prick and RAST – MC mediators, ESR, CRP, TFT, ANA, H. pylori testing, AST, stool tests for parasites and fungus)

Chronic fatigue syndrome (history)

Chronic pelvic pain syndromes [interstitial cystitis, type III chronic prostatitis, vulvadyndia] (cystoscopy and biopsy, prostatic secretion testing)

Familial Mediterranean fever (history, family history, ESR)

Fever of unknown etiology. (history, extensive lab testing)

Fibromyalgia (history, physical, ESR)

Food allergy/sensitivity (history, skin prick tests, RAST, special investigations of biopsies, elimination diet)

Heredity alpha 1 tryptasemia (tryptase level, genetic testing)

Hypereosinophilic syndrome (CBC with differential)

Hypermobile Ehlers Danlos syndrome (history, physical exam)

Hereditary angioedema (family history, C4 level, C1-esterase inhibitor level)

Juvenile rheumatoid arthritis (history, RF, ESR, radiographs)

Lupus erythematosus (history, ANA, ESR)

Sjogren's disease (antibody studies including novel or early Sjogren's antibodies)

Vasculitis (clinical picture, ANA, ESR, and other laboratory studies)

Vascular disorders

Median arcuate ligament syndrome

nutcracker syndrome

pelvic vascular compression syndrome

Infectious diseases - all multi-systemic

Bartonella - can also exacerbate MCAS (PCR and FISH tests)

Mold infection - chronic inflammatory response syndrome - can also exacerbate MCAS (urine aflatoxin test and serum antibody tests)

Syphilis - can also exacerbate MCAS

Tick borne infections - can also exacerbate MCAS (antibody panel)

Tuberculosis (blood and skin tests, radiographs)

Neoplastic diseases

Carcinoid tumor - multi-systemic (24 hr urine 5-HIAA, CT and octreotide imaging)

Intestinal lymphomas multi-systemic (CT studies, endoscopic procedures)

Pancreatic endocrine tumors [gastrinoma, insulinoma, glucagonoma, somatostatin, VIPoma] – multi-systemic (lab determination, imaging studies, endoscopic ultrasound)

Pheochromocytoma – multi-systemic (laboratory studies, CT imaging)

Systemic mastocytosis (tryptase level, bone marrow biopsy)

Neurologic diseases

Cyclic vomiting syndrome (history)

Migraine (history)

Munchausen's syndrome (history)

Postural orthostatic tachycardia syndrome – multi-systemic and exacerbates MCAS (orthostatic pulse exam, tilt table test, autonomic testing)

Serotonin syndrome (history, serotonin level)

Small fiber peripheral neuropathy – multi-systemic (skin biopsy)

Citation: Leonard B. Weinstock, Andrew W. Campbell, Luke Curtis, Jordan Gutovich, "Mycotoxin-Triggered Attacks of Nausea, Vomiting, and Abdominal Pain and Episodes of Pseudo-Obstruction", Universal Library of Medical and Health Sciences, 2024; 2(1): 59-69.

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