Wernicke's Encephalopathy in an Elderly Anorexic Patient

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Introduction

- Wernicke encephalopathy (WE) is a brain disorder resulting from thiamine deficiency
- WE is most commonly found and monitored for in alcoholic patients, but can be due to other situations causing thiamine deficiency ranging from malabsorption to poor intake or even dialysis
- This case demonstrates the importance of maintaining a high index of suspicion for WE in less common high risk groups.

Case Description

History of Present Illness:
A 78 year old female with very little past medical history presented after recurrent falls with weakness. She was noted to have a cardiac arrhythmia at her primary care appointment. History was notable for severely restricted food intake over the last 20 years and other behaviors suggestive of anorexia nervosa.

Exam:
Vitals were notable for occasional tachycardia to low 100s. Telemetry showed frequent PACs. On Physical examination the patient was cachectic and frail appearing, pleasant. She had mild horizontal nystagmus and very subtle limitation of lateral gaze.She required two person assistance with ambulation, gait was unsteady and ataxic. Exam was otherwise normal.

Diagnostic Data

- Labs showed hyponatremia, low protein and albumin, mildly elevated LFTs, borderline microcytic anemia.
- B12 and Folate were elevated/normal
- Monitoring for refeeding syndrome was negative with normal magnesium, phosphate. However, the patient refused NG Tube and only took in PO intake with incomplete calorie counts.
- Telemetry (initially was concerned for Afib on admission) showed frequent PACs

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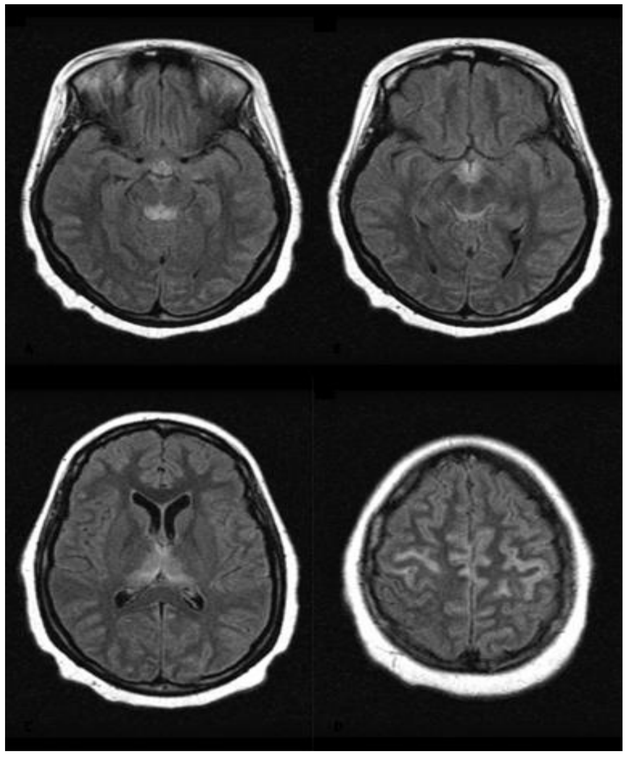
Hospital Course and Further Work-Up

- Workup for the patients weakness revealed subclinical community acquired pneumonia, Previously noted Type III odontoid cervical fracture, and history concerning for poor dietary intake and anorexia nervosa.
- Psychiatry agreed with diagnosis of Anorexia Nervosa, Restrictive Type
- After noting ocular abnormalities on exam, Thiamine replacement was started
- Refeeding with feeding tube was recommended, but the patient refused and was determined to have capacity so she was discharged on a dietary plan with close PCP follow up
- Lab abnormalities on admission (elevated LFTs, hyponatremia, hypoglycemia) improved with monitored oral intake and vitamin supplementation.
- Ataxia improved after hospitalization and falls decreased in frequency



Typical MRI findings of Wernicke's encephalopathy. From top left, clockwise: hyperintensity in periaqueductal midbrain, mammillary bodies, thalamus, and frontal-parietal cortex. Our patient had nonspecific T2/Flair hyperintensities in the periventricular cortical white matter and diffuse cerebral atrophy (not picturesd) . Gradient susceptibility in right basal ganglia was also noted. MRI image from UpToDate Graphic 82317 Courtesy Eric D Schwartz, MD

Discussion

- Wernicke Encephalopathy is a diagnosis frequently considered in cases of alcoholic patients due to the frequency and danger of thiamine deficiency in these patients.
- This case demonstrates another at risk population for nutritional deficiencies including thiamine that can be life threatening if not dangerous.
- There have been case reports before of WE in young patients with anorexia nervosa (1) however instances of elderly females (with our without eating disorders) suffering from thiamine deficiency are far rarer.
- This patient had a psychiatric cause (or contributor) to her severe malnutrition, however malnutrition is a common, complex, and significant issue in elderly patients that has significant prognostic and quality of life implications(2)
- One of the criteria for Wernicke Encephalopathy is ataxia, which contributed to a serious fall in this patient. Falls are common for a number of other reasons in the elderly, so it is not unlikely significant new ataxia could be missed or taken for granted on initial evaluation and, without detailed eye exam, a diagnosis of possible WE is easily missed

Conclusion

This case demonstrates the importance of maintaining a high index of suspicion for Thiamine deficiency and WE, a clinical diagnosis, in malnourished elderly patients and evaluating for ataxia, abnormal extraocular movements, and memory deficits carefully on examination.

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Pulmonary Coccidioidomycosis In A Patient With Subacute Cough

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Introduction

- Coccidioidomycosis is a condition caused by infection with the dimorphic fungi *Coccidioides*
- Most are located geographically in the Southwestern United States and are caused by inhalation of fungal spores
- While most cases in immunocompetent hosts are subclinical, some patients do develop severe complications

Case Description

History of Present Illness:
A healthy 27 year old male from Wyoming who presented with 6 weeks of productive cough and occasional fever. Cough started 2 weeks after a car trip to Disneyland and Las Vegas. Initially treated by PCP for pneumonia with 10 days each of doxycycline, levofloxacin and Augmentin without improvement. X-ray was concerning and sent to our hospital for further workup. Patient denied smoking or illicit drugs. Lives and works in group home as caretaker for patients with disabilities. Patient has multiple pet lizards, dogs, cats.

Exam:
Vitals normal, afebrile.
Bronchial breath sounds in right lung, otherwise normal.

Diagnostic Data

Initial Labs/Imaging:
Labs notable for normal White Blood Count of 8.8, but elevated Eosinophils 11%. Complete Metabolic Panel normal.
Legionella and Streptococcal Urine antigens Negative
HIV negative.
Initial AFB (Acid Fast Bacilli) Culture negative

Chest X-ray showed bilateral consolidations consistent with multifocal pneumonia

CT Chest obtained, showed Right Upper Lobe Cavitary Lesion, multifocal consolidative opacities in RUL and Lingula, concerning for Septic Emboli vs Fungal Pneumonia vs Cavitary Metastasis

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Hospital Course and Further Work-Up

- With history of group home, placed in negative pressure room and 3x AFB cultures obtained. All negative.
- Given concern for septic emboli, Echocardiogram was obtained and was negative.
- On third hospital day sputum cultures grew *Coccidioides Immitis/Posadii* by DNA probe. Additionally, *Coccidioides* Enzyme linked immunoassay by IgM and IgG were positive.
- Confirmatory testing with *Coccidioides Immitis* antibodies positive via immunodiffusion
- Treatment started for 3 months with oral Fluconazole therapy
- At 3 month follow-up, complete resolution of symptoms

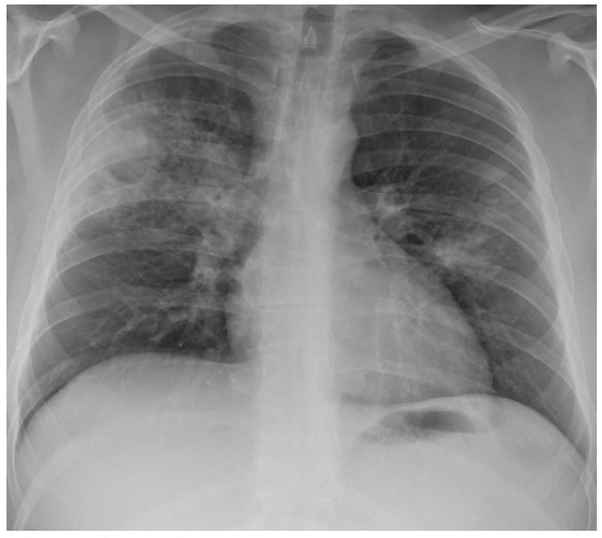

Figure 1. Initial Chest Radiograph with multifocal pneumonia.

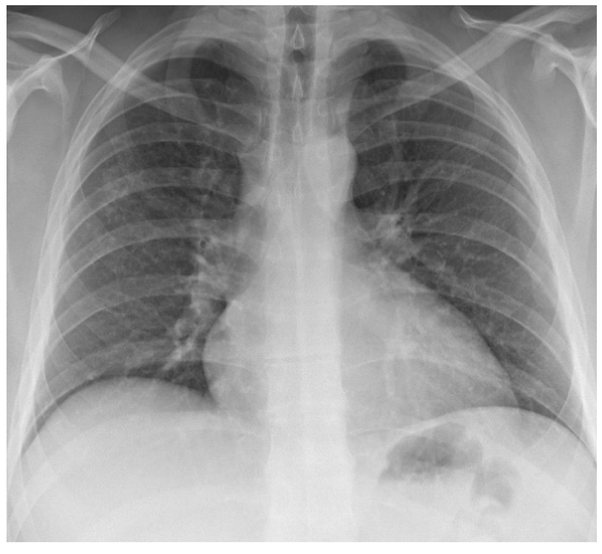

Figure 2. Follow-up Radiograph after 3 months treatment

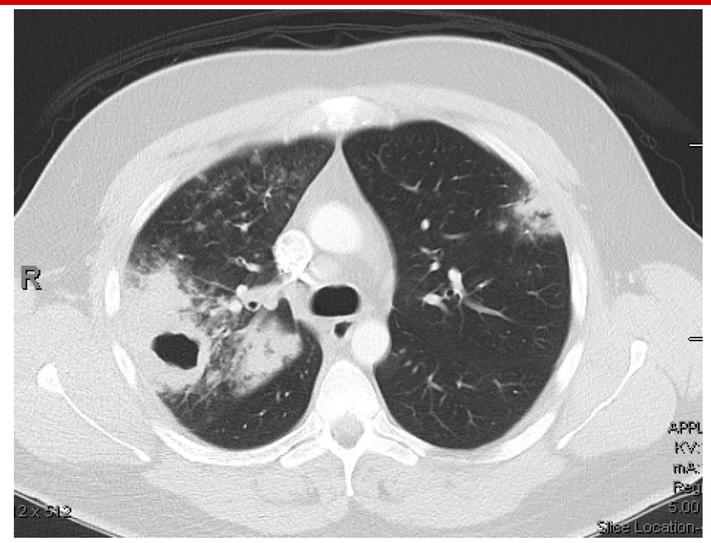

Figure 3. Initial CT scan with multifocal pneumonia and cavitary lesion

Discussion

- Given severe findings on imaging and no known immunocompromised state, the eventual diagnosis was not initially high on differential. Only after the most concerning diagnoses were ruled out (TB, Septic Emboli, Bacterial Pneumonia) that we seriously considered *Coccidioides.*
- After a more thorough and complete travel history was obtained we came to the accurate diagnosis.
- Enzyme linked immunoassay (EIA) testing is highly sensitive for Coccidioides, but confirmation testing with Immunodiffusion is recommended as it is more specific.
- For many patients, treatment is not necessary. Though in patients with more severe disease treatment is recommended with Fluconazole or Itraconazole.

Conclusion

- This case highlights the importance of accurate and in-depth travel history when working up a patient with suspected infection.
- While this patient showed improvement in symptoms and radiographically, some may develop cavities, residual nodules, fibrocavitary pneumonia requiring more aggressive therapy.

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Shiitake mushroom-induced flagellate dermatitis

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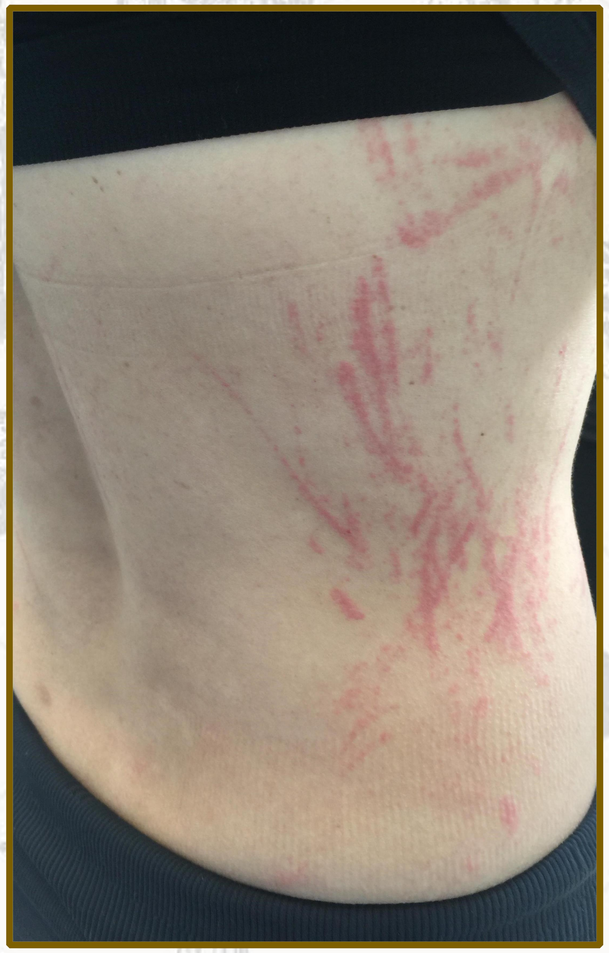
Introduction

Shiitake flagellate dermatitis, also known as "flagellate erythema" and "toxicoderma", is correlated with ingestion of raw or undercooked shiitake mushrooms. It presents as a linear, erythematous eruption, resembling scratch or whiplash marks. The condition was first described in Japan by Nakamura[1] and has since been recorded all over the world, likely in accordance with the rise in Asian agricultural exports.

It is believed that shiitake flagellate dermatitis is a toxic reaction to lentinan, a thermolabile polysaccharide that is found in raw, and lightly cooked shiitake mushrooms. Lentinan stimulates the secretion of interleukin-1, an inflammatory cytokine, which results in vasodilation and hemorrhage[2]. In fully cooked shiitake mushrooms (>145°C), Lentinan is decomposed, which speaks to the lack of flagellate dermatitis following the consumption of cooked shiitake mushrooms. Alternate theories explaining shiitake dermatitis favor an allergic response, however these are less supported, as prick and scratch test results for shiitake mushrooms are generally negative[3].



Case Description

A healthy 42 year old female presented with erythematous, edematous, linear streaks distributed on the trunk resembling whiplash marks (figure 1*).* The eruption had been present for three days and was associated with localized pruritus and stinging. Flagellate dermatitis from shiitake mushrooms was suspected due to her recent ingestion of mushrooms and insistence that she had not scratched the area. The patient later confirmed that she had consumed raw shiitake mushrooms one day prior to the eruption. She was treated with cetirizine 10 mg and triamcinolone 0.1% cream for symptomatic relief. The eruption began improving two days following initiation of the treatment plan, and after two weeks it resolved almost completely.

Discussion

- **Similar erythematous, flagellate eruptions have been observed in response to bleomycin treatment and dermatomyositis, however these presentations often have mucous membrane involvement, which is not seen with shiitake-induce flagellate dermatitis[4].**
- **Diagnosis can be challenging due to variable time course of eruption, which has been documented from 12 hours to several days after mushroom consumption.**
- **Susceptibility to shiitake dermatitis is variable, with an estimated prevalence of approximately two percent[5]. Further studies must be performed to reflect the growing shiitake mushroom market, and resultant exposure.**
- **The popularity of shiitake mushrooms in the United States has grown dramatically in recent years, as Asian cuisine has become a staple of the American culinary landscape[6]. As this mushroom continues to integrate into the Asian-American palate, it is likely that physicians will see more, similar cases. Such a trend calls for increased documentation and discussion of this relatively obscure condition.**

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Montelukast: A Simple, Effective Treatment for GI side effects in patients taking Dimethyl Fumarate for Multiple Sclerosis

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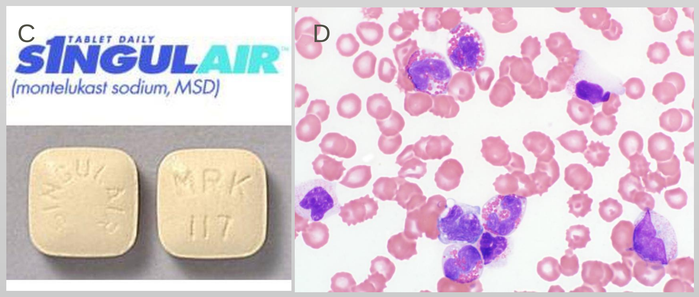
Introduction

Background

- Dimethyl fumarate (DMF, tradename Tecfidera, Images A and B) is an immunomodulatory medication that has been shown to increase the time to relapse in the treatment of multiple sclerosis (MS).

- Clinical trials document that ~40% of patients who begin therapy with DMF experience undesirable GI side effects, such as abdominal pain, nausea, vomiting, diarrhea, and dyspepsia, as well as flushing.[1]
- Additionally, patients who begin treatment with DMF experience a transient increase in mean eosinophil counts during the first 2 months of therapy (Image D). Researchers have suggested that DMF-related GI symptoms could be due to an eosinophilic gastroenteritis-like syndrome.



- Montelukast (tradename Singulair, Image C) is a leukotriene-receptor antagonist that has been used to successfully treat eosinophilic inflammatory disease of the GI tract, and it is suggested that this same treatment may provide relief of DMF-associated GI side effects.[2]

Purpose

- The following is a compelling case of a 67-year-old woman hospitalized for complications of DMF-associated GI symptoms who **experienced near complete resolution of GI symptoms upon treatment with montelukast** and supportive care.

Patient Case

Subjective

CC: Diarrhea

HPI: A 67 yo F with a history of relapsing remitting MS who recently began treatment with DMF was admitted to the hospital complaining of 12 days of "excessive" diarrhea. The patient first noticed 5-7 loose stools/day 2 weeks ago. Patient traveled to the midwest one week ago to visit family where she was evaluated at an urgent care for dehydration. Infectious workup at that time was negative for C. diff, giardia, and cryptosporidium. Symptoms continued to worsen, and at presentation reported **>15 loose stools/day without relief**. Diarrhea was mostly post-prandial, with multiple, loose voluminous stools after meals. Stool is watery and yellow/green. No black, red, or white discoloration. The diarrhea is accompanied by crampy abdominal pain that abates somewhat after each bowel movement. OTC antidiarrheals provide no relief. No vomiting but slight nausea and some dry heaving. No international travel or sick contacts in last month. Patient began MS medication (dimethyl fumarate) 2 months ago, receiving full dose for past month.

PMH: MS, previously taking copxone, now DFM 240mg twice daily. No other medications.

FH: Mother – MS

SH: Retired, monogamous with spouse. No tobacco, alcohol, or recreational drug use.

ROS: Negative except as noted above.

Objective

Vitals: **T:** 37.1 **HR:** 115 **RR:** 24 **BP:** 115/63 **SpO2:** 100%

PE: Exam notes no acute distress, with sunken eyes, dry oropharynx, a fast normal rhythm, 2+ pulses, poor skin turgor, TTP x4 quadrants, and brisk reflexes throughout. Pertinent Labs:

CBC: **WBC 12.0** (PMN 39.5%, Lymps 19.1%, **Eos 33.3%**).

CMP: Na 139, K 3.2, Cl 101, Co2 21, GAP 12, Gluc 147, BUN 35, Cr 1.55.

Ca, Prot, Alb, Total Bili, Alk Phos, AST, ALT, and Lactate Normal.

Clean catch UA: Normal

Urine Cr 74.4, Urine Na 57

Giardia (-), C. diff PCR (-), Stool cx NG, ova/parasites (-).

Patient Case (Cont'd)

Hospital Course

- SIRS physiology resolved in ED after bolus 1L NS x 2.
- Pre-renal AKI on admission (FeNa 0.6%) likely due to GI losses.
- Diarrhea unlikely infectious (afebrile, workup negative). Given known association between DMF and GI symptoms/eosinophilia, DMF was held.
- Patient began treatment with daily montelukast 10 mg per preliminary data suggesting improvement in eosinophilia and GI sx in pts on DMF. Within first 24 hours, the number of stools decreased from >15/day to 4/day and nausea resolved.
- AKI essentially resolved by hospital day 3 and patient was discharged on montelukast 10mg PO daily. Follow up labs ordered and Neurology appt to determine appropriateness of MS therapy.
- Patient ultimately opted to continue DMF regimen with concurrent montelukast therapy. Eosinophil count monitored over next month continued to decrease as shown.

Days post-discharge	Percent Eos	Absolute Eos Count (K/mcL)
DAY 1	46%	5
DAY 6	20%	1.1
DAY 14	7.20%	0.3
DAY 29	3.40%	0.3

Discussion

- Fumaric acid esters have been shown to transiently increase eosinophils by elevating IL-4 through the compound eotaxin, an eosinophil-activating cytokine.
- One Small study (n=21) showed that introduction of montelukast decreased GI symptom scores by 81% in patients taking DMF.[2]
- A phase IV multicenter, double-blind, placebo-controlled clinical trial is currently being conducted to measure GI symptom relief in a larger sample size of MS patients taking DMF.[3]

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A Case of Altered Mental Status: Recent Clinical Diagnostic Guidelines Allow More Timely Treatment for Autoimmune Encephalitis

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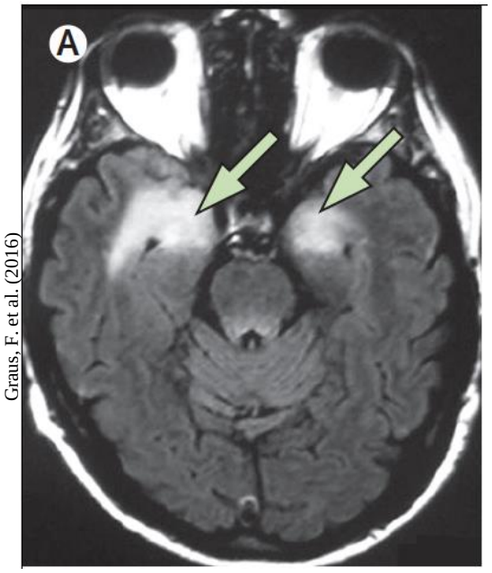
I. Introduction

Encephalitis is non-specific inflammation of the brain, often presenting as altered mental status, and is a common chief complaint encountered in a hospital. There are many causes of encephalitis, with a recently identified sub-type having an autoimmune etiology.

Autoimmune encephalitis is caused by auto-antibodies to neuronal cell-surface or synaptic proteins. The clinical syndrome includes rapid development of confusion, working memory deficit, mood changes, and often seizures. Since this presentation is similar to infectious encephalitis, clinicians often rely on antibody testing for confirmation, however this can delay treatment onset and negatively affect outcomes.



Graus, F. et al. (2016)

(A) Typical MRI of limbic encephalitis with bilateral abnormalities in the medial temporal lobe on T2-W FLAIR sequence; this patient with autopsy-proven limbic encephalitis did not have serum CSF antineuronal antibodies Graus, F. et. al (2016)

II. Case Description

History of Present Illness:
JT is a 24-year-old previously healthy male found down and disoriented on public transport, stating that he has felt "weird" in recent weeks since switching to eCigarettes. He cannot recall the events leading up to his arrival to the ED. He denies drug or alcohol use, past seizures or syncopal episodes, infections, fevers, joint pain, rashes, weakness, numbness, or other recent symptomatology. He admits to feeling anxious, and threatens to "run". He refuses to provide contact information for family members or friends.

Physical Exam:
Vitals: T 37.5 HR 87 RR 16 BP 125/84 SpO2 97% on RA
General: anxious appearing male in no acute distress
HEENT: 3cm superficial laceration on right forehead
Cardiovascular: RRR, no murmurs, rubs, or gallops
Respiratory: lungs clear to auscultation bilaterally, no wheezes, rhonchi or rales
Abdominal: abdomen non-distended. No tenderness to palpation, no rigidity or guarding. **One episode of fecal incontinence on admission**.
Neurological: EOMI, PERRLA. Strength 5/5 throughout, reflexes 2+ throughout.
Psychiatric: Alert & Oriented x3, no overt psychosis, appears mildly paranoid. Anxious, labile affect.

Past Medical/surgical History:
None

Medications & Allergies:
-Meds: None
-Allergies: Hay fever

Social History:
- 2 pack year smoking history, switched to eCigarette 2 weeks ago.
- Denies alcohol or drug use.
- Left polygamous FLDS religion in Southern Utah 2 years ago.
- Works stocking shelves.
- Lives with 3 male co-workers.
- Not sexual active.

Family History:
Not provided

Work up:
(+)
CSF: WBC 17 cells per mm^2. Opening pressure, glucose, and protein WNL
EEG: slow waves isolated to temporal lobe
MRI Brain: FLAIR hyperintensities in medial temporal lobes

(-)
CT Head: normal
Urine and serum toxicology: negative
CSF gram stain & culture: negative
HSV PCR: negative
VZV PCR: negative
HIV ELISA: negative
West Nile: negative
RPR: negative
CMP: WNL
CBC: WNL

III. Diagnostic Criteria

OLD CRITERIA:
Autoimmune antibody titers (which may take > 3 weeks to obtain from a specialized lab); response to steroids

NEW CRITERIA:

A clinical diagnosis of **Definite Autoimmune Limbic Encephalitis** requires the following 4 criteria:*

1. Rapid progression of working memory deficits, seizures, or psychiatric symptoms related to limbic system.
2. Brain MRI abnormalities on T2 FLAIR centered in bilateral medial temporal lobes.
3. CSF WBC >5 cells per mm^2 or EEG with epileptic or slow wave activity involving the temporal lobes.
4. Reasonable exclusion of alternative causes.

IV. Discussion

In the past, the differential diagnosis for patients presenting with encephalitis was complex and encompassed several etiologies, most notably infection. However, several non-infectious causes have recently been identified, some of which have an autoimmune etiology. Previously the criteria for diagnosis of autoimmune encephalitis was too reliant on antibody testing and response to autoimmune therapy, both of which delayed diagnosis. For example, antibody testing results can take weeks to obtain. Also the absence of autoantibodies does not exclude the possibility that a disorder is immune mediated.

With the new criteria, a diagnosis can be confirmed earlier by the clinical picture and MRI findings, and important immunosuppressive therapy can be started without waiting for antibody results.

References

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A Diagnostic Approach to Diarrhea in Immunocompromised

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Introduction

- ***Cystoisospora belli, formerly known as Isospora belli,*** is a spore-forming, obligate intracellular intestinal protozoan that causes cystoisosporiasis, an opportunistic infection characterized by chronic watery diarrhea.
- ***Cystoisospora belli,*** has been reported in patients with cellular immunodeficiencies such as HIV/AIDS, leukemia, and lymphoma.
- In this report we describe a diagnostic approach to severe, persistent watery diarrhea due to cystoisosporiasis in a patient with AIDS and diffuse large B-cell lymphoma (DLBCL).

Case Description

History of Present Illness: A 23-year-old African-born man with AIDS, DLBCL and TPN dependence presented to the emergency department from a care facility with two weeks of worsening watery non-bloody diarrhea.

Patient was admitted to the medical ICU due to severe hypotension that was responsive to fluid resuscitation.

Past Medical History: Patient was first diagnosed with HIV during a work-up for the etiology of DLBCL a year prior to this admission. At that time, he was treated with two rounds of chemotherapy, and achieved remission four months later. Since chemotherapy, he experienced mild chronic watery diarrhea. (consider making this a short list rather than paragraph format)

Medications: Patient has been compliant with his medications. Antiretroviral treatment: Dolutegravir, Emtricitabine, Tenofovir Prophylaxis: Fluconazole, Valganciclovir, Azithromycin, and Trimethoprim-Sulfamethoxazole (TMP-SMX).

Physical exam: Vital signs were notable for hypotension, and tachycardia. Exam notable for cachexia, sunken eyes and a diffusely tender, non-distended abdomen.

Initial Diagnostic Data

- CD4 count was 111 cells/mm^3.
- Blood cultures were negative for bacteria and fungi.
- Viral respiratory panel by PCR and viral respiratory culture were negative.
- Whole blood PCR re-demonstrated CMV viremia.
- Peripheral blood smear and imaging did not show recurrence of DLBCL.
- Cortisol level was normal.
- Stool osmolality and electrolytes were consistent with secretory diarrhea.
- Retroperitoneal ultrasound was unremarkable.
- CT of abdomen and pelvis: Mild diffuse wall thickening of the small bowel.

Further Work-Up

1. Molecular stool studies

Gastrointestinal Bacterial	PCR*
C. diff Toxin B gene by PCR	Not Detected
Shigella/Enteroinvasive E. coli	Not Detected
Salmonella species	Not Detected
Campylobacter jejuni/coli	Not Detected
Campylobacter upsaliensis	Not Detected
Shiga-like toxin 1	Not Detected
Shiga-like toxin 2	Not Detected

Microsporidia	PCR*
Enterocytozoon bieneusi	Not Detected
Encephalitozoon species	Not Detected
Cryptosporidium	Not Detected
Giardia	Not Detected
Entamoeba histolytica	Not Detected
Dientamoeba fragilis	Not Detected
Cyclospora cayetanensis	Not Detected

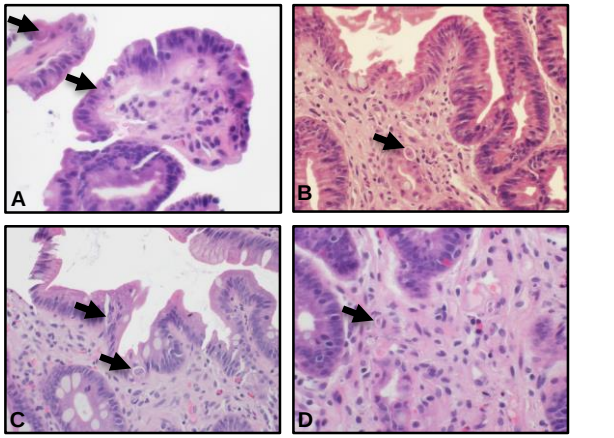
* "A negative result does not rule out the presence of PCR inhibitors in the patient specimen or test-specific nucleic acid in concentrations below the level of detection by this test." ARUP

2. Parasitology examination

Ova and Parasite Exam	Result
O&P, Wet Mount, Fecal	Negative
O&P, Trichrome Stain, Fecal	Negative
Parasitology stain, Fecal (Modified Acid Fast Stain)	Negative

"The ova and parasite exam does not specifically detect Cryptosporidium, Cyclospora, Cystoisospora, and Microsporidia. For Cyclospora and Cystoisospora, refer to Parasitology Stain by Modified Acid-Fast" ARUP

3. Duodenal biopsies with *Cytoisospora* in mucosal epithelium (A-C) and capillaries (D)



Images were provided by Kajsa E. Affolter, M.D.

"CMV immunostain is performed on blocks 4, 5 and 6 and are negative for viral inclusions. Additional special stains include GMS, PASF and AFB, which helped confirm the diagnosis." University of Utah Health, Department of Pathology and ARUP

Discussion

- This patient was treated with a 10-day course of Ciprofloxacin with resolution of diarrhea. Ciprofloxacin was chosen as an alternative therapy due to thrombocytopenia and a history of drug fever with TMP-SMX.
- TMP-SMX is the treatment of choice, so *Cystoisospora* is seen less frequently in those already receiving TMP-SMX for *Pneumocystis jirovecii* prophylaxis [1].
- Although the prevalence of *Cystoisospora belli* is generally low, it is the highest in immunocompromised patients who are foreign-born, such as in this patient [2-5].
- *Cystoisospora belli* usually cannot be detected by routine stool ova and parasite examination so acid-fast staining was requested but also failed to detect the organisms [6]. Overall, the sensitivity and specificity of acid-fast staining is 90 to 100% but *Cystoisospora* is usually the least detected organism because of low prevalence [10].
- PCR analysis for *Cystoisospora* DNA in fecal samples was not available but has previously been shown to help with identification [7].
- Because *Cystoisospora belli* oocysts are not always found in stool, we proceeded with detection of parasites in duodenal aspirate/intestinal biopsy using light microscopy [8,9].

Conclusion

This case illustrates the utility of gastrointestinal biopsy in addition to stool microscopy and acid-fast staining in diagnosing diarrhea of unknown cause.

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Paraneoplastic Guillain–Barré Syndrome

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CASE PRESENTATION

79 year old Male from Tooele, Utah with HTN, CKD IIIa, BPH who initially presented to an outside ED with one month history of progressive bilateral leg pain. Negative initial work up. Patient then reported a ground level fall at home and then experienced rapidly progressive bilateral leg weakness, over one week, to the point of being unable to ambulate, hyporeflexia, distal neuropathy, urinary retention, and bowel paresis.

LABORATORY

CBC, CHEM, Vitamin B12/Folate: wnl
ANA, B6, Copper, CK: wnl, HgA1c 5.6%
Lumbar Puncture: WBC:2, RBC:6, Protein:77, glucose:51. Oligoclonal band profile: wnl Paraneoplastic panel: wnl

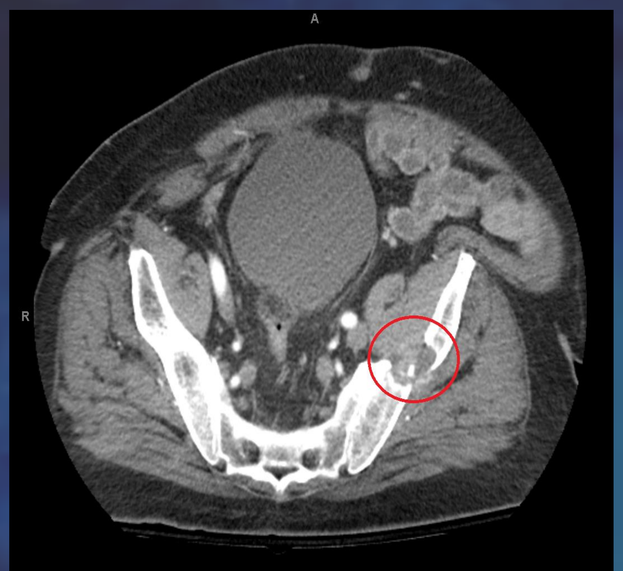
IMAGING

MRI Brain: no abnormalities
MRI C/T/L Spine: no abnormalities
CT Chest: enlarged subaortic and subcarinal nodes.
CT Abdomen/Pelvis: left pubic mass w/fracture and hepatic lesion concerning for metastatic disease

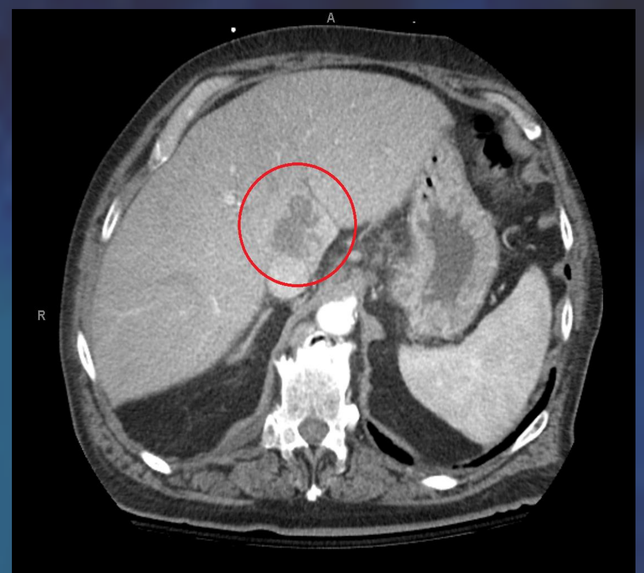
BIOPSY/PATHOLOGY

Immunohistochemistry: CK7 positive, CD20 negative consistent with cholangiocarcinoma.

PELVIC FRACTURE & LESION



HEPATIC LESION



CT Abdomen/Pelvis showing left pubic mass with left pubic ramus fracture and hepatic lesion concerning for metastatic disease

NERVE CONDUCTION STUDIES

NERVE CONDUCTION — nr = no response

NERVE Stimulate Record	AMPLITUDE (mV or uV) R	L	Norm	LATENCY (ms) R	L	Norm
Sural Sensory						
Calf Ankle	nr	nr	(>6)			
Sup Peroneal Senso						
Ankle Foot	nr		(>5)			
Peroneal Motor						
Ankle EDB	nr		(>2)			
Tibial Motor						
Ankle Abd Hal	nr	nr	(>3)			
Ulnar Sensory						
Wrist 5th	nr		(>10)			
Median Sensory						
Wrist Index	nr		(>20)			
Radial Sensory						
Forearm Wrist	nr		(>20)			
Ulnar Motor						
Wrist Hypothen	3.0		(>6)	3.3		(<3.5)
B Elbow "	1.8		(>6)			
A Elbow "	1.6		(>6)			

DIAGNOSTIC CRITERIA Guillain–Barré Syndrome

Required	Supportive
Progressive symmetric weakness of > 1 limb ✓	Sensory symptoms or signs ✓
Hyporeflexia or areflexia ✓	Cranial nerve involvement especially bilateral VII
Progression <4 weeks ✓	Autonomic dysfunction ✓
Symmetric weakness ✓	CSF protein elevation ✓
Exclusionary	CSF cell count < 10/mm3 ✓
Other causes excluded (toxins, botulism, porphyria, diphteria) ✓	Electrophysiologic features of demyelination ✓
	Recovery

FINDINGS

Severe active sensory and motor axonal neuropathy.

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FINAL DIFFERENTIAL

Guillian Barre with Axonal variant: AIDP (acute inflammatory demyelinating polyneuropathy), AMAN (acute motor axonal neuropathy), vs paraneoplastic syndrome.

OUTCOME

We ruled out: Toxic neuropathy, Acute spinal lesions, rheumatologic, stroke, testable paraneoplastic syndromes, myasthenia gravis, lambert eaton, botulism, psychogenic, and rhabdomyolysis.

Based on our testing, patient was diagnosed with GBS with either Axonal variant AIDP (acute inflammatory demyelinating poly-neuropathy), AMAN (acute motor axonal neuropathy).

Patient declined treatment, following new metastatic cancer diagnosis, including treatment for AMAN vs AIDP, which response to treatment would have provided GBS subtype.

LEARNING POINT

Besides the classic presentation of ascending paralysis in demyelinating GBS, clinical variants exist based on the types of nerve fibers involved (motor, sensory, sensory and motor, cranial or autonomic).

This is a case represents a rare presentation of Paraneoplastic Guillian-Barré Syndrome.

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Pneumocystis Jirovecii Pneumonia in a patient with Hypercalcemia

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Introduction

- Pneumocystis Jirovecii (PJP, formerly Pneumocystis Carinii/PCP) is a fungus that causes pneumonia in patient's with impaired cell-mediated immunity.
- This case reviews a 74 year-old female on methotrexate and sirolimus for oral lichen planus who presented to the ICU with worsening hypoxia after fluid resuscitation for hypercalcemia and was eventually found to have PJP pneumonia.

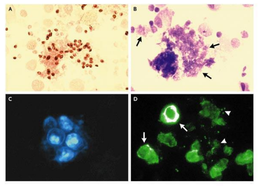

Fig 1:Trophic and cystic forms, with DFA below[1]

Case Description

History of Present Illness:
74 year-old female with type-2 diabetes and oral lichen planus on methotrexate and tacrolimus who presented with 2 weeks of malaise, vomiting, diarrhea, and 10 days of dry cough and dyspnea. Her tacrolimus dose had been increased to 2mg twice daily 6 weeks prior, then subsequently reduced back to 1mg upon initiation of symptoms, as well as a decrease in methotrexate.

Objective:
Vital signs at presentation: Afebrile, blood pressure 110/64, heart rate of 110 beats per minute, breathing 14 times per minute, 94% oxygen saturation on 3 liters/min by nasal canula. She was chronically ill-appearing, with profoundly dry mucus membranes, a normal work of breathing and diffuse crackles, and a mild tenderness throughout her abdomen. She had no lower extremity edema.

Labs and Imaging:
Initial lab work was notable for a WBC 12.9 with 80% neutrophil predominance, glucose of 105, creatinine of 1.1 (baseline 0.8), and a corrected (for albumin) Calcium of 12.9. Her initial chest radiograph showed no evidence of acute cardiopulmonary process.

Hospital Course:
She was given a total of 3.5L of intravenous fluid over the next 24 hours with improvement in her hypercalcemia, but she became progressively more hypoxic and was transferred to the ICU

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Case Synthesis

Assessment upon arrival to ICU:
- 74 year-old immunosuppressed female presenting with hypercalcemia, now with worsening hypoxemic respiratory failure after fluid resuscitation with:
  - markedly increased alveolar-arterial O2 gradient
  - Asymmetric, multifocal hazy opacities with upper lobe predominance on chest radiograph.

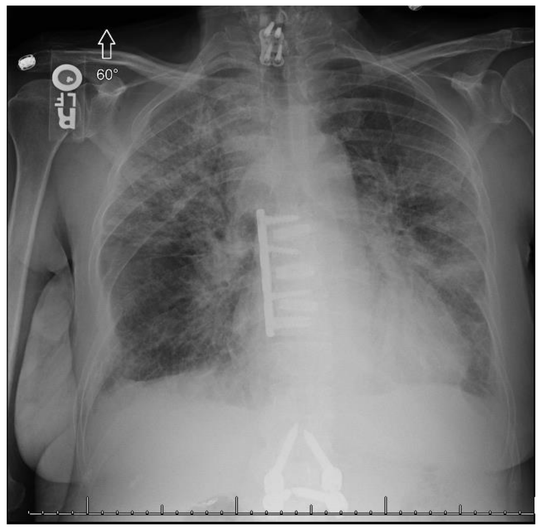

Fig 2: Chest radiograph upon ICU admission. Notable for diffuse bilateral hazy opacities with an upper lobe predominance.

Diagnostic Reasoning and Diagnosis

Differential diagnosis included: Iatrogenic pulmonary edema
Infection (viral, atypical, Tb, fungal), Malignancy, Sarcoidosis

Hypoxia	Hypercalcemia
LDH 327 (ULN 253) Beta-D-glycan positive AFB, fungal cultures negative BNP 633 (ULN 100)	PTH 7 Vit D 25 OH 56 1,25OHD 184.0 (ULN 79.3) PTHrP <2
Multifactorial. Beta-D-glycan can be seen with numerous fungal infections	Suggests excess vitamin D activation

Broncheoalveolar lavage was performed:			
Macrophages	Bronchial lining	Lymphocytes	Neutrophils
10%	6%	59%	25%

Pneumocystis smear was negative, DFA negative, **PCR positive,** supportive of a diagnosis of **Pneumocystis Jirovecii Pneumonia**

PJP Pneumonia

PJP Biology: Cannot be cultured due to tropism for human lungs

Epidemiology: occurs in HIV-negative patient with malignancy, solid organ transplant, and/or immunosuppressive medications, most commonly, cytotoxic immunosuppressives or prednisone.

Symptoms: dry cough and marked hypoxia. Presents acutely in HIV, and sub-acutely in patients without.

Lab and imaging: Elevated beta-D glycan (common to fungal infections) and LDH (likely due to non-specific lung inflammation), 'batwing'-pattern or diffuse hazy opacities on radiograph

Diagnosis: Induced sputum with smear, direct florescent antibody, and PCR is the 1st-line to confirm the diagnosis. However, broncheoalveolar lavage has greater sensitivity and specificity and thus is useful in patients with lower pretest probability.

Note: PCR does not differentiate infection, from colonization, which occurs with unknown frequency. Est. specificity is 92.2%[2]

Treatment: Trimethoprim-Sulfamethoxazole and prednisone 40 to 60mg BID tapered over 21 days if hypoxia is present.

Granulomatous PJP: Numerous atypical pulmonary infections, including PJP, can cause granulomatous reactions that lead to hypercalcemia by excess activation of Vitamin D by macrophages. This may have caused the patient's hypercalcemia, though confirmatory biopsy was not performed[3].

Conclusion

- PJP pneumonia occurs in patients with impaired cell-mediated immunity. The course is often indolent in patients who are not infected with HIV.
- Elevated LDH, Beta-D glycan, hazy perihilar or diffuse infiltrates on chest radiograph suggest the diagnosis, which is confirmed with induced sputum or broncheoalveolar lavage.

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IgG kappa Multiple Myeloma presenting as Hyperviscosity Syndrome

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Introduction

- Hyperviscosity syndrome (HVS) is a potentially life threatening condition caused by increased viscosity of the blood.[1]
- HVS is most commonly caused by Waldenstrom's macroglobulinemia however it can also be associated with multiple myeloma, polycythemia, and leukemia.[1]

Case Description

History of Present Illness:
A 40-year-old male with no past medical history presented to the ED with a severe frontal headache.

Patient had been seen in the ED one week prior with a kidney stone at which time he was found to have normocytic anemia. Was started on oral iron and sent home without further workup.

Further questioning revealed a several week history of severe fatigue, fevers and drenching night sweats. He also reported a 2 week history of frequent epistaxis and oral mucosal bleeding.

Exam:
On admission patient was febrile to 38.5C. Remainder of his vitals were within normal limits. Exam was unremarkable with the exception of some mild gingival bleeding.

Initial Workup

Labs
- WBC 2.6 (ANC 1.9), Hgb 8.3 (MCV 91), Plt 147
- Na 127, Cl 99, K 3.6, CO2 27, BUN 10, Cr 0.98
- AST 57, ALT 40, Bili 0.2, Alb 2.4, Ca 10.4
- Total protein > 14.0
- INR 1.4

Imaging
- CT head showed no evidence of intracranial hemorrhage
- CT abdomen showed non-obstructing L kidney stone

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Hospital Course and Further Work-Up

- Given 1 month history of B symptoms and significant hyperproteinemia a workup for hematologic malignancy was initiated.
  - Blood smear showed "striking rouleaux formation" (Figure 1)
  - IgG 9556, IgM < 5, IgA < 5
  - SPEP showed m spike
  - Serum free light chains - kappa 11.2, lambda <0.16
- Given severity of his headache, mucosal bleeding and degree of IgG level elevation, a diagnosis of hyperviscosity syndrome was made. This was subsequently confirmed based on a serum viscosity level of 3.25 centipoises (normal <1.5)
- Plasmapheresis was performed. Patient's headache resolved.
- Further workup with bone marrow biopsy revealed 80-90% clonal plasma cells in 80% cellular marrow (Figure 2)
- Final diagnosis - IgG Kappa Multiple Myeloma
- Patient will go on to receive induction chemotherapy followed by high-dose chemotherapy and autologous stem cell rescue

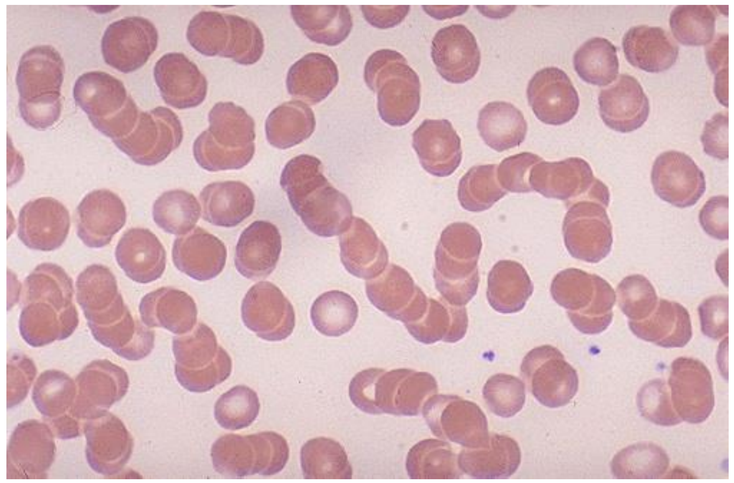

Figure 1. Example of rouleaux formation seen on patient's peripheral blood smear

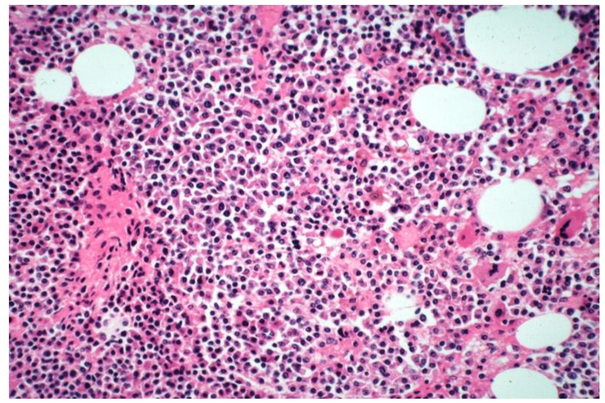

Figure 2. Bone marrow biopsy showing increased plasma cell population [4]

Discussion

- The diagnosis of HVS can be difficult given the non-specific nature of its associated signs and symptoms which include:[2]
  - Constitutional (fatigue, malaise)
  - Bleeding (gingival, mucosal, nasal)
  - Ocular (blurred vision, diplopia)
  - Neurological (headache, vertigo, tinnitus, somnolence)
  - Rarely (seizures, stroke, heart failure, priapism)
- Treatment for HVS includes:[3]
  - Hydration
  - Plasmapheresis
  - Avoidance of transfusions
  - Treatment of underlying cause
- HVS is uncommonly seen in multiple myeloma with only around 2% of patients having evidence of HVS on presentation.[2]

Conclusions

- Internists should be aware of the symptoms associated with HVS and the clinical scenarios in which it should be considered as prompt therapy with plasmapheresis is required to prevent potentially life threatening complications.

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A Classic Case in an Unexpected Place: A Report of Erlichiosis in Central Idaho

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Case Presentation

A 58 year old man with a history of prostate cancer presented to the emergency department with a one week history fever, headache, photophobia, and malaise. Shortly after developing these symptoms, he presented to his local hospital and was admitted with concern for meningitis. LP was unremarkable and additional PCR testing was negative for Lyme, West Nile, and Herpes Virus. His symptoms improved, and he was discharged on Cefdinir and Acyclovir. His symptoms returned, along with bilateral knee pain and productive cough, and he sought a second opinion at our facility. He had not travelled outside of his home state of Idaho in several months, but did report spending time recently at his cabin in central Idaho. Exam was notable for fever to 38.5 degrees, but otherwise unremarkable.

Basic Laboratory Testing on Admission:

-WBC 26 (Leukocytes 5.2%)

-AST 80

-ALT 121

Extensive infectious, malignant, and rheumatologic work-up was undertaken and negative, including lumbar puncture, blood and urine cultures, bronchoscopy including PCR and cultures, ANA, and bone scan. He was treated throughout the admission with broad spectrum antibiotics and defervesced. The patient felt well enough to return home and was discharged without an explanation for his symptoms.

Unfortunately, his symptoms quickly returned and he sought the opinion of a local neurologist who performed additional testing including Erlichia antibodies. IgM was negative but IgG was 1:1024 (normal range <1:64). He had never been treated for Erlichiosis before. He was treated with a 21 day course of Doxycycline and his symptoms resolved and have not recurred.

Discussion

Erlichia is an often suspected cause of fever, malaise, and headache for providers in the southcentral and southeast United States. However, very few cases occur in the western half of the country. It can be a fatal if left untreated, and an index of suspicion is required to make the diagnosis. Historical clues that aid in making the diagnosis include travel to endemic areas and history of a tick bite. Unfortunately, less than half patients remember being bitten. Thrombocytopenia, leukopenia, or elevation of liver enzymes may be present, but vary between individuals. [1]

Diagnosis should be confirmed with laboratory testing. Preferably, serial indirect immunofluorescence assay (IFA) is performed. A fourfold rise is antibody titers is confirmatory for the infection. If taken within the first seven days, IgG is generally.[1] The diagnosis can be suspected when the patient has appropriate symptoms (fever along with one or more of the following symptoms: malaise, headache, anemia, leukopenia, thrombocytopenia, or transaminase elevation) and single elevation of IgG >1:64. [2]

Although not yet reported in humans, cases of Erlichiosis have been reported in canines in Idaho. [3]

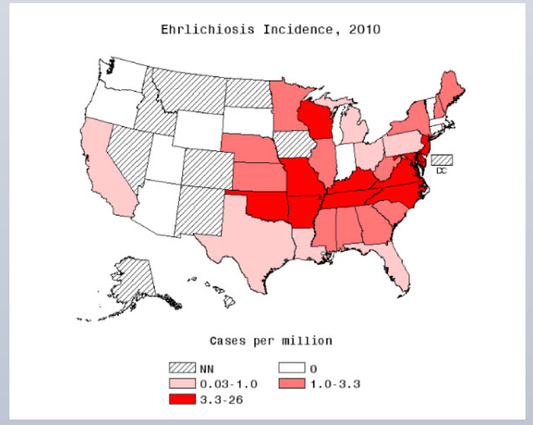

Figure 1: Annual reported incidence (per million population) for E. chaffeensis in the United States for 2010.[1]

Conclusion

While rarely suspected in the western United States, Erlichiosis can be a fatal disease. If suspicion is high despite geographic discrepancies, laboratory testing should be pursued.

Figure 2: Lone Star Tick (*Amblyomma americanum*) is the primary vector for Erlichia spp. [4]

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UNIVERSITY OF UTAH HEALTH CARE

Coxsackievirus: A Case of Sepsis and Rash in an Adult

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Introduction

- This case highlights a presentation of a hospitalized adult with an Enterovirus infection causing sepsis and symptoms similar to hand, foot, and mouth disease (HFMD) including a rash involving the palms, soles, and oral sores.
- HFMD is a common viral exanthem found mostly in children age 5 and younger who are exposed to Enterovirus, particularly Coxsackievirus A16/A6 and Enterovirus 71.
- Typical manifestations of this disease include general malaise, sore throat, and a maculo-papular rash that can involve the palms, soles, and other sites.

Case Presentation

History of Present Illness:
A previously healthy 30-year-old female presented with a headache, neck pain and fever. Initial tests were unremarkable with a normal CBC, CMP, and CSF studies. She was diagnosed with a viral URI and discharged home, but presented 2 days later with the development of a non-pruritic rash on her palms with associated polyarthralgias and a persistent fever. She denied diarrhea or abdominal pain.

Social History:
She works as a researcher in a biochemistry lab. She had one monogamous sexual partner, and denied prior STIs, recent travel, sick contacts or known tick or other bug bites. Her immunizations were up to date.

Diagnostic Data

Vital signs were remarkable for tachycardia, hypotension (90s/60s) and fever with Tmax 102.9˚ F

Exam demonstrated:
- Scattered pinpoint petechiae on hard palate.
- Confluent, erythematous macules on palms, dorsum of hands and soles of feet with scattered petechiae in background. Papules on inner thighs and knees.

Pertinent negatives:
- No lymphadenopathy, meningismus, cardiac murmurs, or lung findings.

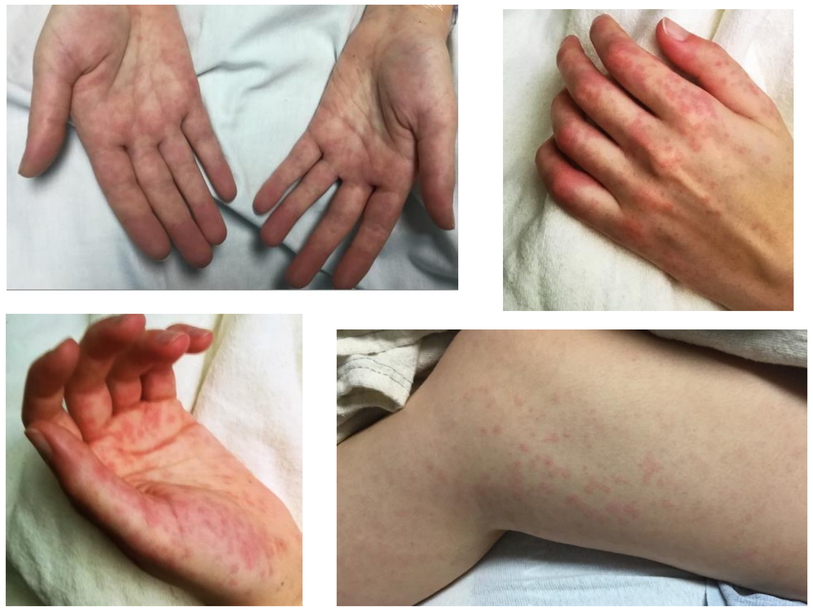

Figure 1. Images of our patient's rash present on her hands and inner thigh

Hospital Course

- Patient's fever and rash gradually improved over her admission. However, she developed pancytopenia after 2 days of hospitalization.
- Lab work returned with negative serologies for rapid flu, respiratory viral panel PCR, EBV panel, Parvovirus IgG & IgM, RPR, Rickettsia IgG & IgM, HIV PCR, Heterophile Ab, GC urine, HSV PCR, and ANA.
- **Lab work was positive for Coxsackie B Ab Type 6 and Echovirus Ab Type 30 at titers of 1:160.**
- Patient's rash and arthralgias were treated symptomatically, and she was discharged home in an improved condition.

Discussion

- This patient presented with a viral prodrome similar to that of HFMD associated with Coxsackievirus. Although she demonstrated a common presentation of this illness, HFMD is not typically seen in adults. This disease affects approximately 11% of exposed adults, however less than 1% of these patients will develop the manifestations of the disease.
- Pancytopenia is rarely seen with Coxsackievirus infections, but has been reported in other cases in the literature.
- Enterovirus infections like in this case are self limited diseases and treated supportively with adequate hydration, antipyretics, and pain control. Interestingly, there are reports of patient improvement after Acyclovir therapy, particularly in severe infections.

Conclusion

This case demonstrates an occurrence of Enterovirus infection manifesting as sepsis with rash and oral ulcers in an adult. This condition should remain on the differential diagnosis for patients presenting with similar viral exanthems, specifically those with an unspecified rash involving the palms and soles.

Contact Information

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Initial Decision Making

Differential Diagnoses:
Based on the distribution of the rash and associated symptoms, viral etiologies were likely including Enterovirus, Coxsackievirus, EBV, Parvovirus, Kawasaki disease, Measles. Other infectious etiologies were considered including Rocky Mountain Spotted Fever, Gonorrhea/Chlamydia, Syphilis, and HIV.

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Hyperammonemia: A Rare but Serious Complication of Bariatric Surgery

UNIVERSITY OF UTAH SCHOOL OF MEDICINE

Josephine Wright MD, Heather Balch MD

Introduction

Obesity is a prevalent, challenging issue in healthcare. Bariatric surgery is well-established as an effective treatment for obesity and its associated comorbidities. However, it also comes with many potential complications, many of which involve nutritional deficiencies. Here, we present a case of hyperammonemia-induced encephalopathy, a rare but potentially fatal complication of gastric bypass surgery, thought to be due to nutritional deficiencies leading to functional deficiencies of urea cycle enzymes.

Case Description

A 35-year-old woman was admitted for progressive altered mental status in the context of multiple recent hospitalizations for various non-specific symptoms including confusion, tremors, emotional lability, personality changes, dizziness, decreased oral intake and occasional vomiting. Ultimately, she was brought in because she was extremely somnolent and no longer interactive. She had no history of preceding fever, chills or any infectious symptoms. Of note, the patient had history of opioid use disorder for which she was on subutex. She otherwise had no history of illicit drug use. She was also on several sedating medications for a variety of mental health issues, including Wellbutrin, hydroxyzine and trazodone. Importantly, patient had history of Roux-en-Y gastric bypass surgery 6 years prior for morbid obesity.

Physical Exam: The patient was obtunded, moaning intermittently, withdrew to pain but otherwise was not interactive and did not follow commands. Pupils were equal, round and reactive to light. Exam was also significant for dry mucus membranes, no nuchal rigidity, abdominal distension and bilateral 1+ pitting edema.

Diagnostic Data

- Initial labs were remarkable for Hgb 7.6, Plt 80, Na 149, CO2 18, TSH 0.21, free T4 wnl, AST 60, ALT 41, total bilirubin 1.4, albumin 3.8, INR 1.4, and ammonia level of 249
- ABG showed pH 7.49, pCO2 26.5, pO2 65, bicarb 20
- Urine toxicology was positive only for MDMA (thought to be a false positive from Wellbutrin)
- APAP <3, negative salicylates and TCA
- CT of the head was unremarkable
- EEG showed diffuse slowing, but no evidence of seizures
- Lumbar puncture showed 18 WBC, with 21% lymphocytes and 30% PMNs, protein 20, glucose 80, with negative gram stain, CSF cultures, HSV/VZV and meningo-encephalitis panel
- Brain MRI showed cytotoxic edema of the corpus callosum, a non-specific finding

Hospital Course and Further Work-up

The patient had no known history of liver disease. It was felt that her elevated INR was due to vitamin K deficiency related to malnutrition. Similarly, her thrombocytopenia was felt to be due to bone marrow suppression due to malnutrition. An abdominal ultrasound showed hepatic steatosis but no evidence of cirrhosis. Further work-up of the elevated ammonia level showed normal vitamin B12, thiamine and folate levels, low pre-albumin, negative acute hepatitis panel. She had a low zinc level. Amino acid levels showed normal citrulline, high glutamine, and low levels of arginine, leucine, methionine, threonine, tyrosine, valine and cysteine. Urine orotic acid was elevated.

The patient was initially empirically treated for meningitis without improvement in mental status. For the hyperammonemia, she was initially treated with lactulose, but eventually required dialysis. Her mental status progressively improved as ammonia levels downtrended. She was started on rifaximin as well as aggressive vitamin repletion with marked improvement in mental status back to baseline by the time of discharge. The patient was also referred to Genetics for possible genetic disorders of the urea cycle, however this turned out to be negative.

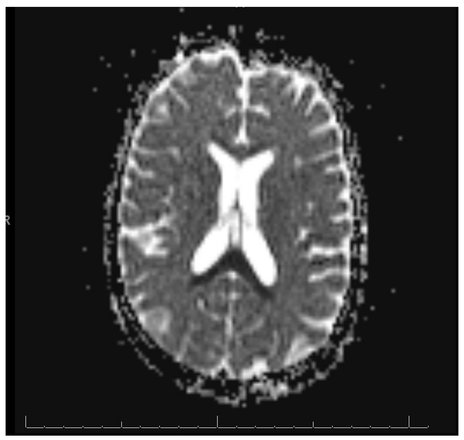

Figure 1. Brain MRI showed cytotoxic edema of the corpus callosum

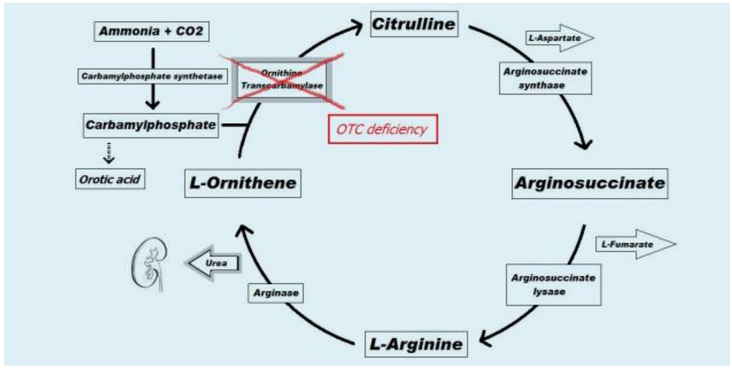

Figure 2. Urea Cycle and OTC deficiency [3]

Discussion

Liver disease is the most common cause of hyperammonemia. Non-hepatic causes include medications (valproic acid, 5-FU), bacterial infections with urease-producing organisms (Proteus, H. pylori, Klebsiella), GI bleed, parenteral nutrition and surgeries such as portosystemic shunts and bariatric surgery. Urea cycle disorders can also lead to hyperammonemia. Several cases have been described in which malnutrition contributed to the unmasking of genetic disorders of the urea cycle in adults undergoing catabolic stress. However, in gastric bypass related hyperammonemia, patients often did not have an identifiable genetic mutation [1-3].

The exact mechanism of hyperammonemia in our patient remains unclear. We suspect that several nutritional deficiencies related to the patient's prior bariatric surgery may have led to the functional deficiency of urea cycle enzymes leading to impaired ureagenesis and subsequent hyperammonemia. Given the patient's elevated urine orotic acid and the pattern seen in her amino acids, her presentation could represent ornithine transcarbamylase (OTC) deficiency. She had low levels of zinc, and zinc deficiency is known to interfere with the enzymatic function of OTC. OTC deficiency is X-linked, so women who are carriers can present later in life with less severe presentations, often times unmasked during increased catabolic states such as starvation or illness.

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Conclusion

This case of hyperammonemia-induced encephalopathy highlights a rare but potentially devastating complication of bariatric surgery. Early diagnosis and aggressive management are imperative. The initial goal of treatment should be to reduce ammonia production and facilitate elimination. In our case, hemodialysis was an effective way to eliminate ammonia in an efficient manner. Long term treatment included protein restriction, vitamin repletion, and oral medication to facilitate nitrogen excretion.

A case of wound botulism associated with skin popping

UNIVERSITY OF UTAH SCHOOL OF MEDICINE

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Introduction

- Wound botulism is a rare but life threatening cause of acute weakness.
- Early recognition of botulism is essential for treatment with anti-toxin.
- This case highlights a rare instance of wound botulism associated with skin popping in an IV drug user.

Case Description

History of Present Illness:
A 58 year old homeless male with a history of IV drug abuse presents with weakness. He was found down and stated that he could not stand up. The weakness had been present for 4 hours prior to presentation. He denied. fevers/chills, cough, SOB, neck pain, back pain, headache, N/V, diarrhea, inflamed or painful joints. He denied any history of trauma. He admitted to regularly skin popping with heroin.

Exam:
Vitals were unremarkable. Pertinent exam findings included: Bilateral ptosis, dysarthria, EOMI, facial sensation intact, smile symmetric, tongue midline, head was drooped forward and the patient was unable to hold his head upright, muscle strength 5/5 in all 4 extremities, reflexes 1+ at bilateral knees, no clonus, small abscesses noted on bilateral upper extremities.

Figure 1. Black tar heroin was found in the patient's pocket

Diagnostic Data

Initial Labs/Imaging:

- CBC, chemistry and liver function tests were normal.
- ESR and CRP were 49 and 8.9 respectively.
- CK was 164. HIV was negative. Blood cultures were negative.
- Urine drug screen was positive for amphetamines, cocaine, and opiates.
- CXR, CT head, and MRI spine were unremarkable. CT of bilateral upper extremities revealed several small subcutaneous and intramuscular abscesses.

Contact Information

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Hospital Course and Further Work-Up

- The patient quickly developed respiratory distress and required intubation. He was admitted to the ICU for supportive care.
- His extraocular eye movements became severely impaired and his muscle strength declined in all four extremities in a symmetric, descending fashion.
- Acetylcholine receptor antibodies returned negative.
- EMG findings were non-specific.
- Botulinum neurotoxin A was detected in his serum.
- The CDC was contacted and the patient was treated with anti-toxin.
- He recovered some of his musculoskeletal strength, however, his strength did not return to baseline.
- He required a tracheostomy in the setting of prolonged intubation secondary to continued respiratory compromise.
- He was ultimately discharged to an extended care facility for continued long term physical therapy.
- The patient's bilateral upper extremity abscesses from skin popping were determined to be the most likely source of his botulism infection.

Transmission Category	Cases
Infant	141
Foodborne	39
Wound	15
Unknown	4

Table 1. Confirmed botulism cases by transmission category - United States, 2015[1]

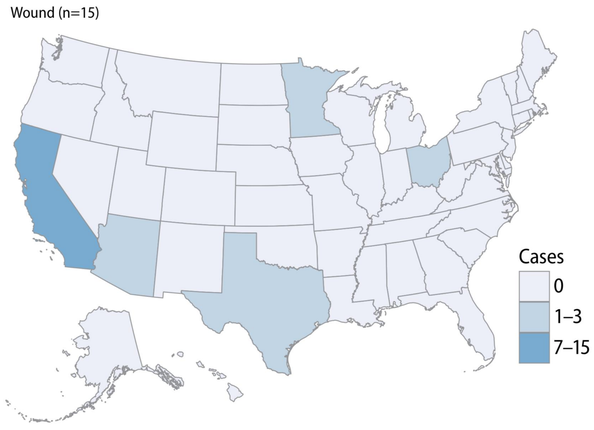

Figure 2. Cases of wound botulism reported to the CDC in 2015[1]

Myasthenia gravis	Poliomyelitis
Lambert-Eaton syndrome	Stroke
Tick paralysis	Heavy metal intoxication
Guillain-Barré syndrome	Epidural abscess

Table 2. Differential Diagnoses

Clinical Presentation of Botulism
Symmetric cranial nerve palsies (ptosis, blurry vision, diplopia, expressionless facies, dysphagia, dysarthria)
Symmetrical descending flaccid paralysis of voluntary muscles
Autonomic symptoms (anhidrosis, dry mouth, postural hypotension)
Paralysis of the pharyngeal muscles and diaphragm that results in respiratory compromise
Deep tendon reflexes progressively disappear
Sensation and intellectual function are preserved

Table 3. Clinical Presentation of Botulism

Discussion

- Botulism is a rare cause of symmetric, descending flaccid paralysis beginning with the cranial nerves and early recognition is essential
- Anti-toxin, which is provided by the CDC, should be given early, ideally within 24 hours of symptom onset, because the anti-toxin arrests the progression of paralysis by binding to toxin molecules that are yet unbound to nerve endings.
- Wound botulism is rare, but when it is seen, it is most commonly seen in IV drug users, especially users of black tar heroin who participate in skin popping.
- Botulism should be included in the differential for all patients with a history of IV drug use who present with weakness.

Conclusion

- Treatment of botulism with anti-toxin is time sensitive, thus early recognition of botulism is essential. Botulism should be considered in the differential for all patient's with a history of IV drug use who present with weakness.

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Family Satisfaction in the Huntsman Cancer Hospital Intensive Care Unit

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Abstract

Purpose: A quality improvement survey project to assess family satisfaction in the Huntsman Cancer Hospital Intensive Care Unit (HICU). **Hypothesis:** Family members of patients admitted to the HICU will ascribe higher importance but lower satisfaction to questions regarding communication and information needs than to other questions about quality of patient care. Exploring family satisfaction will help identify areas of improvement for the HICU. **Methods:** A validated version of the Family Satisfaction in the ICU survey (FS-ICU)[1] was used to survey 34 family members of patients discharged from the HICU. **Results:** Questions about information needs generally had high importance and high satisfaction. Specific targets for improvement (questions with high importance and low satisfaction) include frequency of communication, emotional support, pain management, and supportive inclusion in decision making.

Background

- ICU patients are often unable to fully participate in the decision making process because of their critical illness.
- Family members thus play an important role in assessing the quality of care
- Previous studies have suggested that family members of critically ill patients consider fulfillment of information needs among the most important yet least satisfying aspects of the ICU experience.[2,3]

Methods

- FS-ICU Questions:

Q1	HICU Handout	Q13	Atmosphere of waiting room
Q2	Coordination of care by HICU staff	Q14	Frequency of communication with providers
Q3	Concern and caring by HICU staff	Q15	Ease of getting information
Q4	Management of pain	Q16	Understanding of information
Q5	Management of breathlessness	Q17	Honesty of information
Q6	Management of agitation	Q18	Completeness of information
Q7	Consideration of family member needs	Q19	Consistency of information
Q8	Emotional support for family member	Q20	Inclusion in decision making
Q9	Skill and competence of nurses	Q21	Support in decision making
Q10	Frequency of communication with nurses	Q22	Control over care
Q11	Skill and competence of providers	Q23	Time to have questions answered
Q12	Atmosphere of HICU		

Results

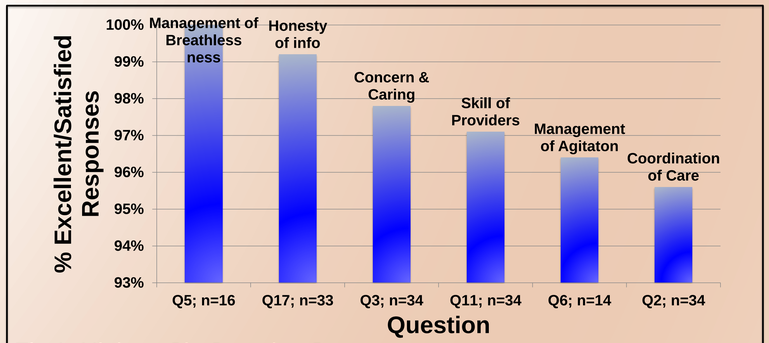

Fig 1: Highest Six Question Scores

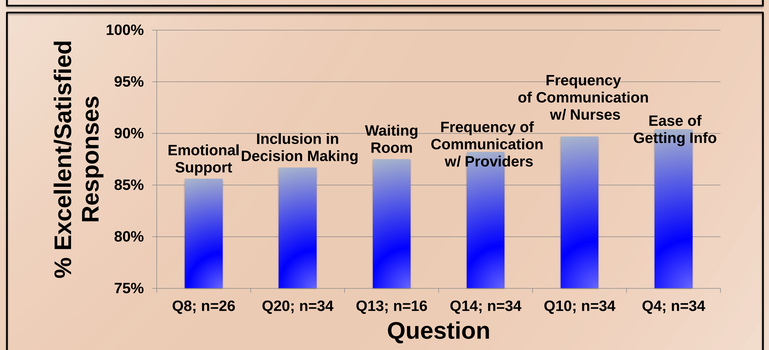

Fig 2: Lowest Six Question Scores

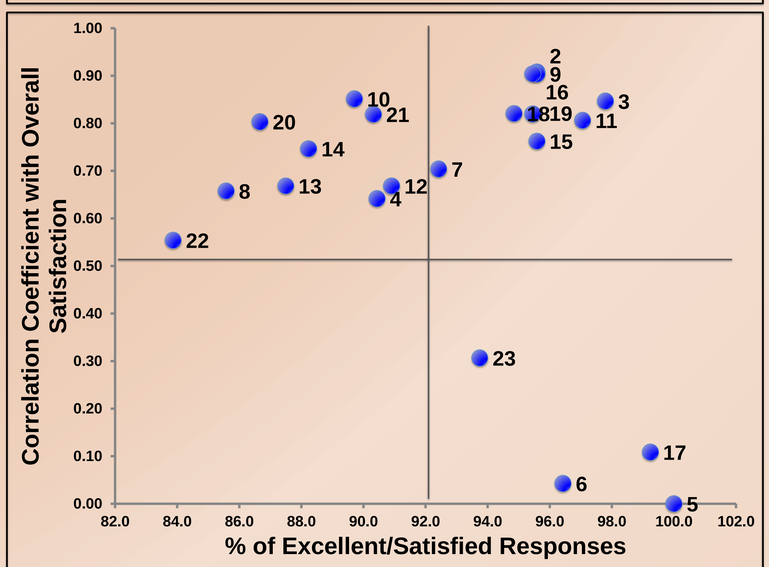

Fig 3: Performance-Importance Grid. Importance can be determined by correlation of items with overall satisfaction.[4] Satisfaction for a given item can be determined by rate of excellent responses. Items with high importance but low satisfaction (top left quadrant) represent potential improvements that would most increase overall satisfaction.

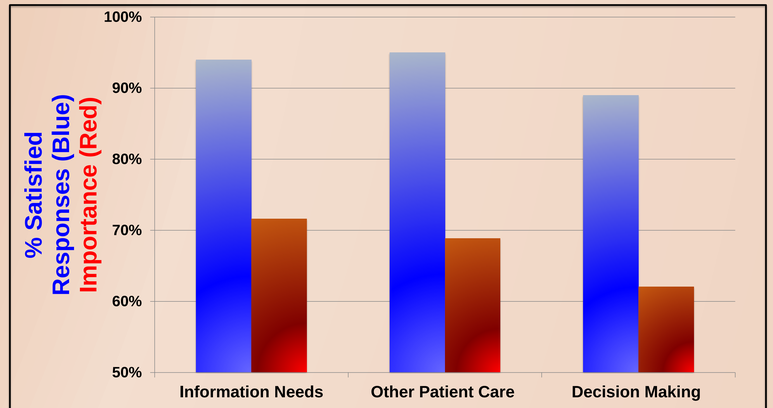

Fig 4: Satisfaction and Importance by Question Category. The questions with highest average importance (correlation with overall score) pertained to information needs. The questions with the highest average satisfaction pertained to other patient care.

Discussion

In order to be useful, data about family satisfaction must identify areas for quality improvement. These improvement opportunities can be prioritized by the relative importance and satisfaction of survey items.[4] The results of this survey show that family members of ICU patients consider communication and information sharing to be some of their most important needs. They are often dissatisfied with the extent to which they are included in the decision making process. The leadership team at the HICU can improve the experience for families by increasing the frequency of communication between both doctors and nurses with families. They can offer more emotional support, particularly to patients in severe pain. Finally they can reach out to families at key decision points to help them feel more empowered and included. In their comments, many family members of critically-ill patients expressed their amazement and gratitude at the high quality of care they had received. There is always room for improvement, however, and this survey shows some good places to start.

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A new role for NAP1L1 in human platelets under septic conditions

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Abstract and Introduction

Platelets (PLT) are anucleate and traditionally considered incapable of nuclear functions. In contrast to this preconceived notion, nuclear proteins were detected in human PLT. Nevertheless, for most of these proteins it is unclear if traditional nuclear or alternatively assigned functions are performed, a question we wanted to address by the presented study. Here, we demonstrate that the nuclear assembly protein 1 like 1 (NAP1L1) acts as a chaperone for mitochondrial (MT) proteins in human PLT. We found that NAP1L1 mRNA is expressed in CD34⁺-cell-derived megakaryocytes (MEGS) and human PLT using next generation sequencing and PCR techniques. In addition, we were able to unequivocally demonstrate that PLT and MEGS contain NAP1L1 protein in different, so far unknown, isoforms. While NAP1L1 did not co-localize with classic PLT granule content, it was mainly cytoplasmic in MEGS and PLT. Co-IP experiments using anti-NAP1L1 antibodies and subsequent massspectrometry analysis revealed that a small set of proteins does interact with NAP1L1. We focused on a prominent 70kDa protein which was identified and verified as dihydrolipoyllysine-residue acetyltransferase (DLAT)-PDC-E2. DLAT is part of the MT pyruvate-dehydrogenase multi-enzyme complex, nuclear encoded and needs to be transported from the cytoplasm to the MT after being translated. DLAT plays a crucial role in maintaining cellular respiration and energy production by linking glycolysis with the citric acid cycle and therefore promoting ATP-synthesis via the respiratory chain. Since altered MT function is a hallmark of infectious syndromes, we analyzed NAP1L1 and DLAT expression in PLT isolated from septic and dengue virus infected patients. NAP1L1 showed an increased expression pattern in patient samples (RNA and protein level), whereas DLAT demonstrated decreased levels. These results indicate that NAP1L1 plays an important role as chaperon maintaining mitochondrial function under stress-situations.

Methods

Cells. Washed human platelets were isolated from septic patients and healthy individuals, removing contaminating leukocytes by CD45 bead selection at the platelet rich plasma stage (PRP). The negatively selected platelets were resuspended in M199 serum-free culture medium for all studies.

Western Blots (WB). WB were performed as previously described using standard methods and monoclonal as well as polyclonal antibodies against NAP1L1.

Protein Co-Immunoprecipitation (Co-IP). Platelets were isolated as described above. Platelet protein Co-IP was performed using the Universal Magnetic Co-IP kit according to the manufacturer's protocol.

PDH activity assay. Platelets were lysed post isolation and PDH activity was determined according to the manufacturers protocol (Abcam).

Immunocytochemistry. After cell isolation, paraformaldehyde (2% final) was added directly to the washed platelets or MEGS (being cultured on fibrinogen coated coverslides) to maintain the native morphology of the cells, as previously described. Fixed platelets were subsequently layered onto vectabond™ coated coverslips using a cytospin centrifuge. Platelets or MEGS were permeabilized and counterstained. Expression pattern were analyzed using CellProfiler automated software.

Results

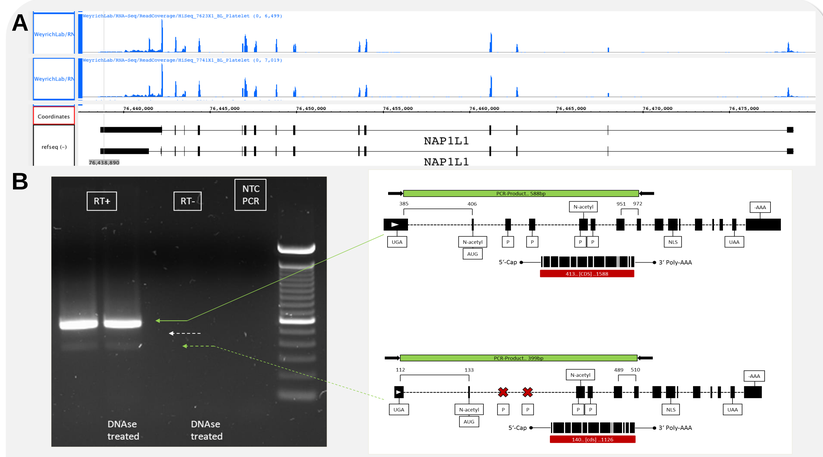

Figure 1. NAP1L1 mRNA is expressed in human platelets. (A) Platelet RNA was isolated and analyzed using next generation sequencing. The graph indicates the read coverage in RPKM (blue graph, for two independent platelet samples). The gene architecture is indicated by the black trace, demonstrating different predicted isoforms. **(B)** On the left, a representative PCR is shown, demonstrating differentially expressed isoforms in human platelets.

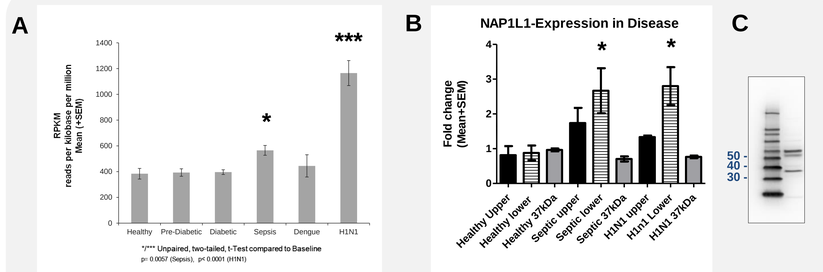

Figure 2. NAP1L1 expression changes in health and disease. (A) Platelet RNA from healthy donors, and diseased groups was isolated and analyzed using next generation sequencing. The graph indicates the read coverage in RPKM. Significant differences between the groups are indicated. **(B)** The graph depicts differential expression pattern of NAP1L1 protein isoforms in human platelets, changing with respective diseases (mean±SEM, single asterisk: p<0.05). **(C)** Representative Western Blot is shown indicating the different NAP1L1 isoforms expressed in human platelets.

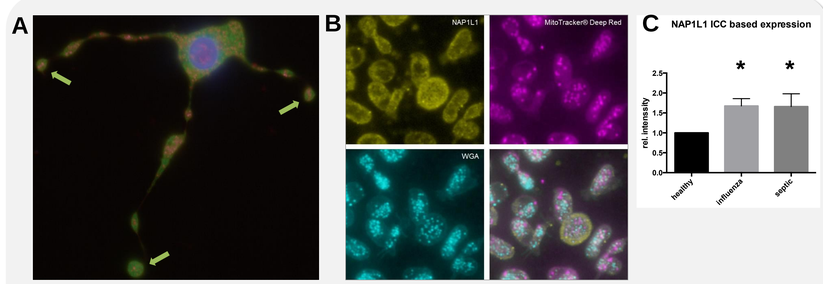

Figure 3. NAP1L1 protein is shifted to developing proplatelet extensions and demonstrates limited co-localization with platelet granules and mitochondria. (A) NAP1L1 (green) localized in a day 14 CD34+ derived megakaryocyte (proplatelet extensions marked by arrows, granules indicated by WGA (wheat germ agglutinin, red). This demonstrates that megakaryocytes invest their NAP1L1 protein pool into their progeny, the platelets. **(B)** NAP1L1 localized in human platelets (green). Mitochondria (magenta) and alpha-granules (turquoise) are highlighted, indicating that the majority of NAP1L1 does reside in the cytoplasm. **(C)** Bar graph indicating the relative amount of NAP1L1 in platelets isolated from healthy donors or diseased individuals (mean±SEM, single asterisk: p<0.05).

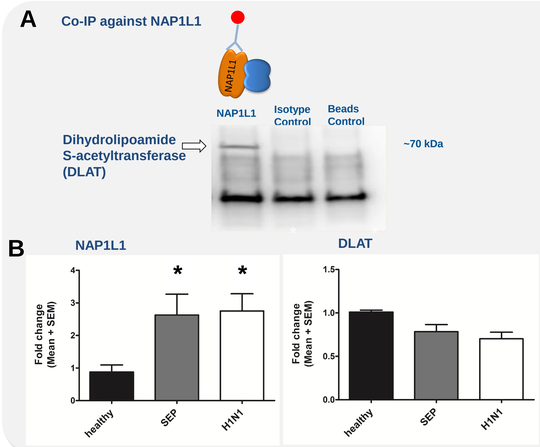

Figure 4. NAP1L1 binding partner was isolated by co-IP and identified as DLAT, a subunit of pyruvate-dehydrogenase – multienzyme complex, using LC-MS/MS. Isolated human platelets were lysed and anti-NAP1L1 co-IP was performed. **(A)** The schematic demonstrates the approach to co-IP. The SDS gels depicts the specific co-IP (left lane) and the appropriate negative controls (middle and right lane). **(B)** Co-IPs were performed for lysed platelets isolated from healthy donors, septic and H1N1 infected individuals. NAP1L1 expression and the amount of interacting DLAT were analyzed using Western blot techniques. Date are shown for NAP1L1 (left) and DLAT (right), and expressed as fold change over healthy levels (mean±SEM). Single asterisk: p<0.05.

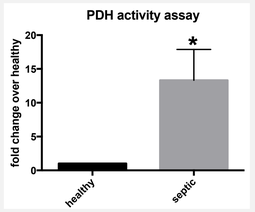

Figure 5. Pyruvate-dehydrogenase – multienzyme complex (PDH) activity was analyzed in health and disease. Isolated human platelets were lysed and PDH activity assay was performed. The bar graph depicts fold change activity of PDH in platelets isolated from healthy vs. septic individuals. Date are expressed as mean±SEM. Single asterisk: p<0.05.

Discussion and Conclusion

•Here we can clearly demonstrate, that NAP1L1 transcript isoform expression, is significantly higher PLT isolated from septic patients, when compared to the control cohorts. This could be an indicator for a mechanism, where MEGS exposed to the septic milieu, modulate the PTL transcriptome due to external cues.

•For the first time, (DLAT)-PDC-E2 was identified to directly interact with NAP1L1. DLAT, a nuclear encoded protein which needs to be transported from the cytoplasm to the mitochondria, plays an essential role in linking glycolysis with citric acid cycle and therefore, promoting ATP-synthesis via the respiratory chain. A function, PLT are highly dependent on.

•Increased NAP1L1 mRNA and protein levels might lead to increased chaperone function for DLAT-shuttling - and therefore, strengthen PLT mitochondrial function - to help overcome sepsis-induced cellular stress, as demonstrated in our PDH activity assay data set.

•Future studies using overexpression and knock-down of NAP1L1 in cell-systems and murine models are planned, accompanied by functional mitochondrial readouts, and disease challenges. In addition, subgroup analysis of sepsis patients with higher vs. lower mortality should shed additional light on NAP1L1 chaperone activity and its relevance. Furthermore, this should enable us to demonstrate that mitochondrial dysfunction, due to altered chaperone function on a molecular level, strongly correlates with sepsis severity and outcome in humans.

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Evaluation of the Likelihood of Specific Press Ganey® Outpatient Medical Practice Survey Questions to Receive a Perfect Score

HEALTH UNIVERSITY OF UTAH

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Department of Orthopeadics

Background:

The Press Ganey® Outpatient Medical Practice Survey (PGOMPS) is a common patient-reported questionnaire used to measure satisfaction with outpatient healthcare in the United States. These scores may be directly linked to physician reimbursement in certain practice settings.

The PGOMPS is composed of 25 questions: 10 are specific to the interaction and perception of the care provider, 7 specifically rate the nursing and office staff, and 8 relate to the practice in general.

Objective:

Our aim was to determine the frequency of patient satisfaction with each individual question to highlight potential areas for improvement in outpatient satisfaction. Our null hypothesis was that the frequency of satisfaction would be similar for each PGOMPS question.

Methods:

We reviewed all PGOMPS total scores for new patient visits between 1/2014 and 12/2016 for all specialties at a tertiary academic health center.

Table 1

* MD Friendliness/Courtesy	84.20%
* MD Spoke Using Clear Language	83.33%
* MD Confidence	82.61%
* MD Likelihood To Recommend	82.57%
* Likelihood Recommend Practice	81.86%
Cleanliness Of Practice	81.44%
* MD Explained Problem Or Condition	80.84%
*MD Concern For Your Questions/Worries	80.67%
Nurse Friendliness	80.44%
* MD Effort To Include You In Decisions	80.08%
Courtesy Registration Staff	78.41%
Staff Work Together	78.02%
Concern For Privacy	77.64%
* MD Information About Meds	77.49%
* MD Instructions Followup Care	77.17%
* MD Time Spent	76.75%
Staff Protect Safety	76.24%
Sensitivity To Needs	75.80%
Nurse Concern	74.30%
Ease Of Scheduling Appointment	65.33%
Convenience Of Office Hours	61.06%
Ability To Get Desired Appointment	59.66%
Ease Of Getting On Phone	58.69%
Information About Delays	56.75%
Wait Time	55.98%

* Questions directly related to the provider

Due to large ceiling effects in the PGOMPS, satisfaction was defined as a perfect total score. The percent of perfect scores for each question was calculated.

Results

95,026 patients met inclusion criteria. The percent of perfect scores for each question is provided in Table 1.

Conclusions:

- Our results suggest that the majority of patients who complete the PGOMPS are satisfied with their provider, demonstrating that room for improvement is limited with provider-specific portions of the clinic interaction.
- The majority of dissatisfaction, or low-scoring questions, pertain to aspects of the clinic that may not be directly within the control of providers.
- Administrators and leaders of health care teams should consider these results when seeking ways to improve patient satisfaction scores.

Out-of-pocket drug costs, shared decision making, and ticagrelor use in acute myocardial infarction

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Abstract

Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor is a cornerstone of acute myocardial infarction (AMI) treatment. The PLATO trial showed a mortality benefit with ticagrelor versus clopidogrel. Our goal was to determine the association between out-of-pocket drug costs and ticagrelor selection among patients hospitalized for AMI after engaging in a shared decision making process (SDM). Of 143 AMI patients loaded with ticagrelor, 70 (49%) switched to clopidogrel following a SMD process. The median, monthly ticagrelor co-payment was $268.29 (interquartile range [IQR] $45-$350) for switchers, versus $18 (IQR $6-$24) for non-switchers (p<0.001). Patients with co-payment greater than or equal to $100 per month were 3.4 times more likely to switch to clopidogrel (RR 3.41, 95% CI 2.12 to 5.47), compared to patients with co-payment less than $100 per month. In summary, half of AMI patients switch from ticagrelor to clopidogrel when cost was taken into account during a SDM process.

Introduction

- DAPT with aspirin and a P2Y12 inhibitor is a cornerstone of AMI treatment, and the PLATO trial showed a mortality benefit with ticagrelor versus clopidogrel[1,2].
- Ticagrelor is more potent, has faster onset, and quicker elimination when compared to clopidogrel[2].
- University of Utah Health implemented a standardized treatment algorithm in February 2015 where patients presenting with AMI were preferentially loaded with ticagrelor.
- Ticagrelor may be cost prohibitive to some patients, costing as much as >$300 per month depending on patient insurance coverage.
- Shared decision making (SDM) is a way to ensure medical care is in line with patients' values and preferences, and is associated with increased patient knowledge, improved risk perceptions, and better medication adherence[3].
- Our goal was to determine the association between out-of-pocket drug costs and ticagrelor selection among patients hospitalized for AMI after engaging in a SDM process.

Table 1. Characteristics of patients loaded with ticagrelor for AMI who continue this medication or switch to clopidogrel prior to discharge

Variable	Patients who continued ticagrelor (n=73)	Patients who switched to clopidogrel (n=70)	p-value
Age (yr±SD)	62.8±11.6	62.8 +/- 12.1	
Monthly Copayment Cost (median cost $, IQR)	18, 6-24	268.29, 45-350	<0.001**
Monthly Copayment Cost (%)			<0.001**
$0-$100	80.8	22.9	
$100+	11.0	47.1	
Missing Cost Data	8.2	30.0	
Primary payer (%)			0.001**
Medicare/Private/Other	91.8	70.0	
Medicaid/Self	8.2	30.0	
Race (%)			0.301
White	87.7	81.4	
Non-white	12.3	18.6	
Medical Illnesses (%)			
Atrial Fibrillation	5.5	8.6	0.469
Current or recent smoker within one year	19.2	37.1	0.017**
Hypertension	56.2	47.1	0.280
Dyslipidemia	64.4	54.3	0.219
Currently on dialysis	1.4	4.3	0.290
Diabetes mellitus	24.7	27.1	0.734
Prior myocardial infarction	13.7	24.3	0.106
Prior heart failure	9.6	14.3	0.386
Prior PCI	15.1	22.9	0.234
Prior CABG	5.5	8.6	0.469
Cerebrovascular disease	5.5	10.0	0.311
Prior Stroke	5.5	5.7	0.201
Peripheral arterial disease	5.5	4.3	0.741
STEMI or STEMI equivalent	71.2	67.1	0.596
Transferred from outside facility	24.7	28.6	0.596
PCI during hospitalization	97.3	90.0	0.074
Oral anticoagulant at discharge	1.4	12.9	0.007**

Figure 1. Cohort development diagram

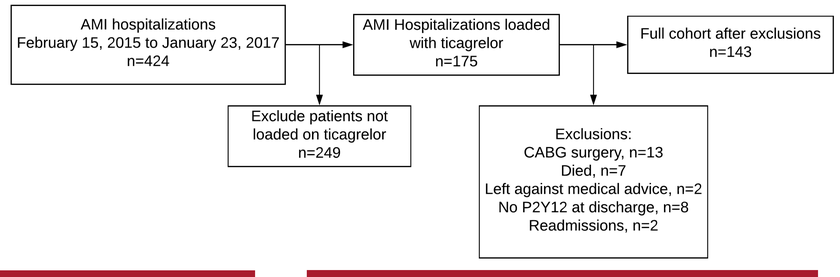


Figure 2. Ticagrelor cost, all patients

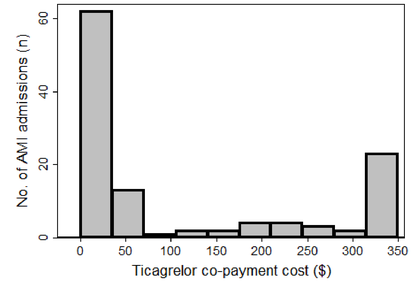


Figure 3. Ticagrelor cost, patients who continued ticagrelor

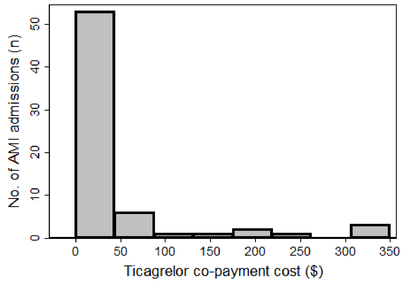
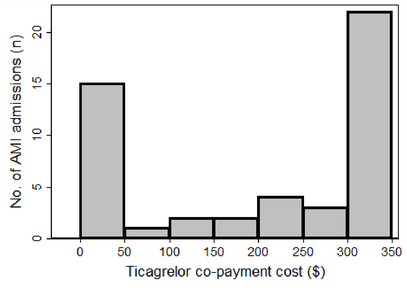


Figure 4. Ticagrelor cost, patients who switched to clopidogrel



Methods

- Retrospective cohort study of all AMI hospitalizations at our facility between February 15, 2015 and January 23, 2017.
- Exclusions: not loaded on ticagrelor, CABG surgery, died, left against medical advice, did not require P2Y12 on discharge, and readmissions.
- A pharmacist-patient SDM process occurred within 24 hours after first dose of P2Y12 inhibitor.
- Repurposing of ACTION Registry® data including key demographics and clinical variables.
- Analysis utilized Wilcoxon rank-sum tests and Poisson multivariable regression to determine the association between cost and switching. A sensitivity analysis was used to account for missing cost data.

Results

- Half of patients switched from ticagrelor to clopidogrel after SDM.
- Comorbid conditions between the groups were similar aside from atrial fibrillation and use of oral anticoagulants.
- Patients with out-of-pocket cost ≥$100/month were 3.4 times more likely to switch to clopidogrel (RR 3.41, 95% CI 2.12 to 5.47), compared to patients with out-of-pocket cost <$100/month.
- Sensitivity analysis excluding missing cost data found that the adjusted RR of switching to clopidogrel was 1.25 (95% CI 1.17 to 1.34) for every $50 increase in monthly out-of-pocket cost.

Discussion

- Our finding that half of AMI patients switch from ticagrelor to clopidogrel following a SDM process is critical to balancing evidenced based medicine with real-world application.
- Shared decision making is a way to ensure medical care is in line with patients' values and preferences, and is associated with increased patient knowledge, improved risk perceptions, and better medication adherence[3].

Limitations:

- Lack of availability of ticagrelor at rural referral hospitals and need for fibrinolytics contributed to only a 41% adherence to ticagrelor protocol.
- Use of a non-standardized SDM script; decision aids that incorporate accepted measures of risk and benefit are needed in the future. Ongoing efforts should include standardized discussions and systematic assessment for all patients

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