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.

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.

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 or 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 extracranial movements, and memory deficits carefully on examination.

References

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

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/Posadis 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

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.

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References
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.

References

http://hriotech.ashpublications.org/content/18/3/490.full.pdf.html.
Montelukast: A Simple, Effective Treatment for GI side effects in patients taking Dimethyl Fumarate for Multiple Sclerosis

James Gardner BS1, Casey Fenger BS1
1. University of Utah, School of Medicine

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.

**Purpose**
- The following is a compelling case of a 67-year-old woman hospitalized for complications of DMF-associated GI side effects upon treatment with montelukast and supportive care.

**Subjective**

CC: Diarrhea

HP: 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 cpoxone, 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 Bill, 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

**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 unlikley 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 apt to determine appropriateness of MS therapy.
- Patient ultimately opted to continue DMF regime with concurrent montelukast therapy. Eosinophil count monitored over next month continued to decrease as shown.

**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.
- 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.

**References**


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.

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.
- **Neurological:** normal strength, normal reflexes, no rigidity or guarding. **One episode of incontinence on admission.**

**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 mm². Opening pressure, glucose, and protein WNL
EEG: slow waves isolated to temporal lobe
MRI Brain: FLAIR hyperintensities in medial temporal lobes

**References**
A Diagnostic Approach to Diarrhea in Immuno compromised

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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/mm3.
• Blood cultures were negative for bacteria and fungi.
• Viral respiratory panel by PCR and viral respiratory culture was 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.
• Retropertioneal ultrasound was unremarkable.
• CT of abdomen and pelvis: Mild diffuse wall thickening of the small bowel.

Further Work-Up

1. Molecular stool studies

<table>
<thead>
<tr>
<th>Gastrointestinal Bacterial</th>
<th>PCR*</th>
<th>Microsporida</th>
<th>PCR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. diff Toxin B gene by PCR</td>
<td>Not Detected</td>
<td>Enterocytozoon bieneusi</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Shigella/Enteroinvasive E. coli</td>
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<td>E. histolytica species</td>
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<tr>
<td>Salmonella species</td>
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<tr>
<td>Campylobacter jejuni/coll</td>
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<td>Campylobacter species</td>
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<tr>
<td>Campylobacter upsaliensis</td>
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<td>Campylobacter species</td>
<td>Not Detected</td>
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<tr>
<td>Shiga-like toxin 1</td>
<td>Not Detected</td>
<td>Shiga-like toxin 1</td>
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<tr>
<td>Shiga-like toxin 2</td>
<td>Not Detected</td>
<td>Shiga-like toxin 2</td>
<td>Not Detected</td>
</tr>
</tbody>
</table>

* "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

<table>
<thead>
<tr>
<th>Ova and Parasite Exam</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>O&amp;P, Wet Mount, Fecal</td>
<td>Negative</td>
</tr>
<tr>
<td>O&amp;P, Trichrome Stain, Fecal</td>
<td>Negative</td>
</tr>
<tr>
<td>Parasitology stain, Fecal (Modified Acid Fast Stain)</td>
<td>Negative</td>
</tr>
</tbody>
</table>

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

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

“CMV Immunostain is performed on blocks 4, 5 and 6 and are negative for viral inclusions. Additional special stains include GMS, PASD and AF, which helped confirm the diagnosis.” University of Utah Health, Department of Pathology and ARUP

Discussion

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

References


Contact Information

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Images were provided by Kajsa E. Altiero, M.D.
**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% 

**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.

**FINDINGS**

Severe active sensory and motor axonal neuropathy.

**OUTCOME**

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

Based on our testing, patient was diagnosed with GBS with either Axonal variant AIDP (acute inflammatory demyelinating polyneuropathy), 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 Guillain-Barré Syndrome.

**REFERENCES**


Pneumocystis Jirovecii Pneumonia in a patient with Hypercalcemia

Brian Locke, MD

Department of Internal Medicine, University of Utah, Salt Lake City, Utah

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 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.

Case Description

History of Present Illness:

74-year-old female with type-2 diabetes and oral lichen planus 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.

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.

Diagnostic Reasoning and Diagnosis

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

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-acute 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, bronchoalveolar 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%

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.

Conclusion

- PIP 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 bronchoalveolar lavage.

References

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

The diagnosis of HVS can be difficult given the non-specific nature of its associated signs and symptoms which include:

- 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:

- 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.

Introduction

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

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

- 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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Discussion

- The diagnosis of HVS can be difficult given the non-specific nature of its associated signs and symptoms which include:
  - 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:
  - 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.

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.

References

2. Talamo, G et al. Clinical lymphoma, myeloma and leukemia, 2010;10(6), 464-468
4. Images from Pathology Education Informational Resource (PEIR) Digital Library
A Classic Case in an Unexpected Place: A Report of Erlichiosis in Central Idaho

Emily Signor, MD, Katie Lappe, MD

Department of Internal Medicine, University of Utah, Salt Lake City, UT

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.

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. 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.

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

References

Coxsackievirus: A Case of Sepsis and Rash in an Adult  
Lindsey Snyder MD, Amanda Breviu MD  
Department of Internal Medicine, University of Utah, Salt Lake City, Utah

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 maculopapular rash that can involve the palms, soles, and other sites.

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.

Case Presentation

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.
- No serology for rapid flu, respiratory viral panel PCR, EBV panel, Parovirus IgG & IgM, RPR, Rickettsia IgG & IgM, HIV PCR, Heterophile Ab, GC urine, HSV PCR, and ANA.

Differential Diagnoses:

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

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, Parovirus 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 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

References

- Andreoni AR, Colton AS. Coxsackievirus B5 associated with hand-foot-mouth disease in a healthy adult. JAAD Case Reports. 2017; 3(2):156-158.
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 liability, 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, with profuse sweating 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.

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.

References


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

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² University of Utah Medical School, Salt Lake City, Utah

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 up right, muscle strength 5/5 in all 4 extremities, reflexes symmetrical, no clonus, small abscesses noted on bilateral upper extremities.

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.

Diagnostic Data

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

<table>
<thead>
<tr>
<th>Transmission Category</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>141</td>
</tr>
<tr>
<td>Foodborne</td>
<td>39</td>
</tr>
<tr>
<td>Wound</td>
<td>15</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
</tr>
</tbody>
</table>

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 extracranial 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.

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.

References

Family Satisfaction in the Huntsman Cancer Hospital Intensive Care Unit

Thomas Anderson; Estelle Harris, MD
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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) 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.

Methods

- FS-ICU Questions:
  
  | Q1 | ICU Handout | Q13 | Atmosphere of waiting room |
  | Q2 | Coordination of care by ICU staff | Q14 | Frequency of communication with providers |
  | Q3 | Concern and caring by ICU 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 ICU |

Results

Focus on improvement opportunities by prioritizing questions with highest importance (red) and lowest satisfaction (blue) as shown in Figs 1-3. The questions with the highest average importance (correlation with overall satisfaction) are shown in Fig 4.

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. 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.

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. 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 use this 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.

References:


Acknowledgments: Thanks to Doug Clapp, Wade Carter, and all the HICU staff!
A new role for NAP1L1 in human platelets under septic conditions

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5Department of Internal Medicine at the George E. Wahlen Salt Lake City VAMC* in Salt Lake City, Utah

Abstract and Introduction

Platelets (PLT) are anucleate and traditionally considered incapable of nucleic acid function. 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 (MEG5) and human PLT using next generation sequencing and PCR techniques. In addition, we were able to unequivocally demonstrate that PLT and MEG5 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 ditydrodipopyline-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 mitochondrial matrix after being translated. DLAT plays a crucial role in maintaining celluar respiratory enzymes 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 fibronogen 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 RPMI (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. 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 localized to mitochondrial granules. (A) NAP1L1 (green) localized in a day 14 CD34**-derived megakaryocyte (red arrow), and co-localizes with cytochrome c (magenta) and alpha-granules (turquoise). (B) NAP1L1 localizes in developing proplatelet extensions. (C) NAP1L1 localizes in the platelet aggregate. (D) NAP1L1 co-localizes with mitochondrial granules. The data indicate that NAP1L1 is associated with mitochondrial granules.

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 PLT 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 the 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.

Contact Information

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**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>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td>* MD Friendliness/Courtesy</td>
</tr>
<tr>
<td>* MD Spoke Using Clear Language</td>
</tr>
<tr>
<td>* MD Confidence</td>
</tr>
<tr>
<td>* MD Likelihood To Recommend</td>
</tr>
<tr>
<td>* Likelihood Recommend Practice</td>
</tr>
<tr>
<td>Cleanliness Of Practice</td>
</tr>
<tr>
<td>* MD Explained Problem Or Condition</td>
</tr>
<tr>
<td>*MD Concern For Your Questions/Worries</td>
</tr>
<tr>
<td>Nurse Friendliness</td>
</tr>
<tr>
<td>* MD Effort To Include You In Decisions</td>
</tr>
<tr>
<td>Courtesy Registration Staff</td>
</tr>
<tr>
<td>Staff Work Together</td>
</tr>
<tr>
<td>Concern For Privacy</td>
</tr>
<tr>
<td>* MD Information About Meds</td>
</tr>
<tr>
<td>* MD Instructions Followup Care</td>
</tr>
<tr>
<td>* MD Time Spent</td>
</tr>
<tr>
<td>Staff Protect Safety</td>
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<tr>
<td>Sensitivity To Needs</td>
</tr>
<tr>
<td>Nurse Concern</td>
</tr>
<tr>
<td>Ease Of Scheduling Appointment</td>
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<tr>
<td>Convenience Of Office Hours</td>
</tr>
<tr>
<td>Ability To Get Desired Appointment</td>
</tr>
<tr>
<td>Ease Of Getting On Phone</td>
</tr>
<tr>
<td>Information About Delays</td>
</tr>
<tr>
<td>Wait Time</td>
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</tbody>
</table>

* 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–$24) for non-switchers ($<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.3
• University of Utah Health implemented a standardized treatment algorithm in February 2015 where patients presenting with AMI were preferentially loaded with ticagrelor.4
• 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.5
• 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 medicine or switch to clopidogrel prior to discharge

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients who continued ticagrelor (n=23)</th>
<th>Patients who switched to clopidogrel (n=70)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>62.8±11.6</td>
<td>62.8±12.1</td>
<td></td>
</tr>
<tr>
<td>Monthly Copayment Cost (median cost, IQR)</td>
<td>18.6-24</td>
<td>268.29-45-350</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>$51150</td>
<td>80.8</td>
<td>22.9</td>
<td>&lt;0.001**</td>
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<td>$100</td>
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<tr>
<td>Missing Cost</td>
<td>8.2</td>
<td>30.0</td>
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<tr>
<td>Primary payer (%)</td>
<td></td>
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<tr>
<td>Medicare/Private/Other</td>
<td>91.8</td>
<td>70.0</td>
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<tr>
<td>Medicaid/No</td>
<td>8.2</td>
<td>30.0</td>
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<tr>
<td>Race (%)</td>
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<td>81.4</td>
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</tr>
<tr>
<td>White</td>
<td>12.3</td>
<td>18.6</td>
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<tr>
<td>Non-white</td>
<td>87.7</td>
<td>81.4</td>
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<td>Medical Illness (%)</td>
<td>10.2</td>
<td>37.1</td>
<td>0.037**</td>
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<td>Atural Filtration</td>
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<td>8.6</td>
<td>0.469</td>
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<td>Current or recent smoker within one year</td>
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<tr>
<td>Hypertension</td>
<td>56.2</td>
<td>47.1</td>
<td>0.280</td>
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<td>27.1</td>
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<td>Prior myocardial infarction</td>
<td>53.7</td>
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<td>Prior PCI</td>
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<td>14.3</td>
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<td>Prior CABG</td>
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<td>Cerebrovascular disease</td>
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<td>Prior Stroke</td>
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<td>5.7</td>
<td>0.201</td>
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<td>Peripheral arterial disease</td>
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<td>4.3</td>
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<td>STEMI or ESMI equivalent</td>
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<td>67.1</td>
<td>0.596</td>
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<td>Transferred from outside facility</td>
<td>24.7</td>
<td>28.6</td>
<td>0.556</td>
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<td>PCI during hospitalization</td>
<td>97.3</td>
<td>90.0</td>
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<td>Oral anticoagulat at discharge</td>
<td>1.4</td>
<td>12.9</td>
<td>0.007**</td>
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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.6
• 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

References