Cancer Center Advertising to the Public
Ten-Year Trends in Prevalence and Spending

Laura B. Vater MPH¹, Julie M. Donohue PhD², Seo Young Park PhD³, Yael Schenker MD, MAS⁴

¹Indiana University School of Medicine, ²Department of Health Policy and Management, University of Pittsburgh Graduate School of Public Health, ³Department of Biostatistics, University of Pittsburgh, ⁴Division of General Internal Medicine, Section of Palliative Care and Medical Ethics, University of Pittsburgh

Background

• The American public is exposed to advertising by cancer centers through a variety of media outlets
• Little is known about the primary sources of cancer center advertising, or the intensity of advertising spending

Objective

• To describe cancer center advertising (top advertisers, expenditures, frequency, media outlets, and target audience) from 2005 to 2014
• To obtain expenditure and prevalence data from Kantar Media, an independent media-monitoring agency
• To adjust all expenditure data to 2014 U.S. dollars using the Consumer Price Index
• To determine the 20 leading advertisers in 2014 in terms of spending

Methods

• Obtained expenditure and prevalence data from Kantar Media, an independent media-monitoring agency
• Assessed data across six U.S. media markets: television, magazines, radio, newspapers, billboards, and the Internet
• Adjusted all expenditure data to 2014 U.S. dollars using the Consumer Price Index
• Determined the 20 leading advertisers in 2014 in terms of spending

Main Findings

Trends in advertising spending, 2005 to 2014

- Television
- Print Media
- Internet Search
- Internet Displays
- Radio
- Billboards

Data are from Kantar Media (www.kantarmedia.com). All data were adjusted to 2014 U.S. dollars using the Consumer Price Index. *Print media includes magazines and newspapers. **Kantar Media did not report Internet search advertising data until 2010.

Cancer centers with the highest spending in 2014

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cancer Center</th>
<th>U.S. Location(s)</th>
<th>Total 2014 Advertising Spending (millions of dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cancer Treatment Centers of America</td>
<td>Atlanta, GA, Chicago, IL, Philadelphia, PA, Phoenix, AZ, Tulsa, OK</td>
<td>101.7</td>
</tr>
<tr>
<td>2</td>
<td>MD Anderson Cancer Center</td>
<td>Houston, TX, Albuquerque, NM, Camden, NJ, Gilbert, AZ</td>
<td>13.9</td>
</tr>
<tr>
<td>3</td>
<td>Memorial Sloan-Kettering Cancer Center</td>
<td>New York, NY</td>
<td>5.1</td>
</tr>
<tr>
<td>4</td>
<td>Fox Chase Cancer Center</td>
<td>Philadelphia, PA</td>
<td>2.5</td>
</tr>
<tr>
<td>5</td>
<td>Texas Oncology</td>
<td>Austin, TX, Dallas, TX, Fort Worth, TX, Houston, TX</td>
<td>3.4</td>
</tr>
<tr>
<td>6</td>
<td>Huntsman Cancer Institute</td>
<td>Salt Lake City, UT</td>
<td>2.2</td>
</tr>
<tr>
<td>7</td>
<td>Sutter Cancer Center</td>
<td>Sacramento, CA, Roseville, CA</td>
<td>2.1</td>
</tr>
<tr>
<td>8</td>
<td>Dana-Farber Cancer Institute</td>
<td>Boston, MA</td>
<td>1.8</td>
</tr>
<tr>
<td>9</td>
<td>CCIS Oncology</td>
<td>Buffalo, NY</td>
<td>1.5</td>
</tr>
<tr>
<td>10</td>
<td>Winthrop NYC CancerCare</td>
<td>New York, NY</td>
<td>1.3</td>
</tr>
<tr>
<td>11</td>
<td>COH Proton Center</td>
<td>Chicago, IL</td>
<td>1.3</td>
</tr>
<tr>
<td>12</td>
<td>Seattle Cancer Care Alliance Clinic</td>
<td>Seattle, WA</td>
<td>1.0</td>
</tr>
<tr>
<td>13</td>
<td>H. Lee Moffitt Cancer Center</td>
<td>Tampa, FL</td>
<td>0.9</td>
</tr>
<tr>
<td>14</td>
<td>Edward Cancer Center</td>
<td>Chicago, IL</td>
<td>0.9</td>
</tr>
<tr>
<td>15</td>
<td>Florida Cancer Specialists &amp; Research Institute</td>
<td>Orlando, FL, Orlando, FL, Tallahassee, FL, Tampa, FL</td>
<td>0.9</td>
</tr>
<tr>
<td>16</td>
<td>Fred Hutchinson Cancer Research Center</td>
<td>Seattle, WA</td>
<td>0.8</td>
</tr>
<tr>
<td>17</td>
<td>University Of Florida Proton Therapy Institute</td>
<td>Jacksonville, FL</td>
<td>0.8</td>
</tr>
<tr>
<td>18</td>
<td>Kennedy Cancer Center</td>
<td>Philadelphia, PA</td>
<td>0.8</td>
</tr>
<tr>
<td>19</td>
<td>Swedish Cancer Institute</td>
<td>Seattle, WA</td>
<td>0.7</td>
</tr>
<tr>
<td>20</td>
<td>James Cancer Hospital</td>
<td>Columbus, OH</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Number of advertisements purchased by cancer centers, 2005 to 2014

<table>
<thead>
<tr>
<th>Annual advertisements per media channel</th>
<th>Direct-to-consumer advertising</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internet Displays</td>
<td>15,091</td>
</tr>
<tr>
<td>Television</td>
<td>52,774</td>
</tr>
<tr>
<td>Local Radio</td>
<td>7,114</td>
</tr>
<tr>
<td>Print Media</td>
<td>1,116</td>
</tr>
<tr>
<td>Total Advertisements</td>
<td>76,095</td>
</tr>
</tbody>
</table>

Data on annual advertisement frequency are from Kantar Media (www.kantarmedia.com).

Results Summary

• Between 2005 and 2014, 890 cancer centers advertised to the public
• Total advertising spending increased from $54 million in 2005 to $173 million in 2014
• The number of advertisements increased nearly ten-fold in the same period, from 76,095 to 708,934
• Twenty cancer centers accounted for 86% of total advertising spending in 2014
• In 2014, 35 NCI-designated cancer centers advertised, ranging from $1,000 to $13.9 million

Limitations

• Some data were not available from Kantar Media: physician-directed marketing, medical center advertising for cancer services, or community events.
• Our findings likely underestimate total advertising spending.

Conclusions

• Spending on cancer center advertising has more than tripled since 2005
• A majority of advertising efforts are concentrated among centers not designated by the National Cancer Institute
• Health care providers should help patients evaluate cancer center ads and make informed decisions about where to seek cancer care
INTRODUCTION

- Angioedema occurs in 0.1-1% of patients taking ACE-inhibitor therapy.
- Classically presents as asymmetric, non-pitting edema of skin and subcutaneous tissues.
- Typically involves face, lips, and tongue causing respiratory compromise.
- Atypical presentations can often go unrecognized.

CASE PRESENTATION

A 43 y/o African-American Female presents with her 4th episode of abdominal pain associated with nausea, bilious vomiting, and diarrhea. She describes the pain as non-radiating, crampy 10/10 pain located in the epigastrium. Her previous episodes are similar in nature and have lasted 48-72 hours. She is completely asymptomatic between episodes.

- No fevers, weight loss, dysphagia, hematochezia/melena.
- Past Medical History: Hypertension (well-controlled)
- Surgical History: None
- Medications: Lisinopril 5mg daily for >5 years.
- Social History: Denies alcohol, smoking, and illicit drugs.

- Physical Examination
  - T: 97.8F, HR 88, BP 129/82, RR18, SpO2 98% on room air
  - Patient in moderate distress. Abdomen diffusely tender, with no rigidity or guarding. Normal bowel sounds.

- Previous Abdominal Pain Work up:
  - 2 previous hospitalizations for abdominal pain that resolved spontaneously
  - CT abdomen/pelvis: small bowel intussusception and segmental wall thickening of the small bowel jejunum and colonic splenic flexure.
  - Patient thought to have Crohn’s disease and was on steroid therapy for a few days before a colonoscopy demonstrated normal ileocolonic mucosa.

Table 1. Comprehensive work up to rule out competing etiologies

<table>
<thead>
<tr>
<th>Labs</th>
<th>Result</th>
<th>Disease process evaluated</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>5.6</td>
<td>Infection</td>
</tr>
<tr>
<td>Lactate</td>
<td>2.7</td>
<td>Ischemia</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>1.45</td>
<td>Inflammation</td>
</tr>
<tr>
<td>Blood calcium</td>
<td>46</td>
<td>Periperal Blood Smear</td>
</tr>
<tr>
<td>SPP</td>
<td>Negative</td>
<td>Leukemia/lymphoma, vasculitis, cryoglobulinemia</td>
</tr>
<tr>
<td>CRP</td>
<td>Negative</td>
<td>Periperal Blood Smear</td>
</tr>
<tr>
<td>ANA</td>
<td>Negative</td>
<td>Autoimmune disease</td>
</tr>
<tr>
<td>ANCA</td>
<td>&lt;1.20</td>
<td>Vasculitis</td>
</tr>
<tr>
<td>Anti-dsDNA</td>
<td>Positive</td>
<td>Lupus</td>
</tr>
<tr>
<td>Anti-histone antibody</td>
<td>Negative</td>
<td>Drug-induced lupus</td>
</tr>
<tr>
<td>Hepatitis C Antibody</td>
<td>Non-reactive</td>
<td>Cryoglobulinic vasculitis</td>
</tr>
<tr>
<td>Urine chorophobilinogen</td>
<td>&lt;3</td>
<td>Acute intermittent porphyria if &gt;10</td>
</tr>
<tr>
<td>C1-INH function</td>
<td>110%</td>
<td>Hereditary/acquired angioedema if &lt;68%</td>
</tr>
<tr>
<td>C1-INH serum level</td>
<td>B1</td>
<td>Hereditary angioedema(l) or acquired C1INH deficiency if &lt;2</td>
</tr>
<tr>
<td>C4 complement</td>
<td>35</td>
<td>Hereditary/acquired C1INH deficiency if &lt;10</td>
</tr>
</tbody>
</table>

RESOLUTION

Patient managed supportively. Her pain resolved in roughly 72 hours, similar to her previous episodes.

After successfully ruling out other etiologies, the patient was thought to have ACE-inhibitor induced visceral angioedema. Her lisinopril was switched to amlopidine and she was subsequently discharged. She continues to follow up as an outpatient without recurrence of her abdominal pain.

LEARNING OBJECTIVES

1) General characteristics of ACE-I induced angioedema

- Up to 68% of angioedema cases related to ACE-inhibitors.
- Variable time to onset, from hours to years after start of therapy.
- Episodes last 48-96 hours even if ACE-I is not held.
- Risk of ACE-I induced angioedema 4.5x higher in African-Americans than Caucasians.
- The trigger is unknown.

2) Pathway for ACE-I induced angioedema

- ACE-I blocks bradykinin degradation.
- Bradykinin increases vascular permeability and vasodilation.

Figure 1. Bradykinin degradation pathway.

3) ACE-I visceral angioedema

- Unknown incidence due to rarity.
- Recurrent episodes of acute, self-limited abdominal pain associated with nausea, vomiting, and watery diarrhea. Patients are hemodynamically stable.
- Typical CT findings: marked submucosal edema, mild dilatation and thickening of small bowel mucosa, patent vasculature, and preservation of luminal transit.
- Involved segment usually >10cm, involves the ileum and/or jejunum, and has adjacent ascites.
- Diagnosis of exclusion: Must exclude infection, ischemia, IBD, trauma, malignancy, vasculitis, radiation enteritis, hereditary or acquired C1 esterase inhibitor deficiency.

Figure 2. Typical findings on CT abdomen/pelvis

Impression: Long segment of small bowel wall thickening/edema in jejunum (arrow) with adjacent ascites. Patent vasculature.

4) Treatment

- If airway involved: Antihistamine, epinephrine, glucocorticoids, and intubation.
- If isolated visceral involvement: supportive care, withdrawal of offending agent.
- Is switching to an ARB safe? Two case series demonstrated recurrence of angioedema when patients were switched to an ARB. Rate of 7.7% and 32%.

WORKS CITED

**BACKGROUND**

- Proton pump inhibitors (PPIs) are the 3rd-highest selling drug class in the United States.
- Previous studies demonstrated that 35-61% of outpatients are on acid suppression therapy without an appropriate indication.
- Chronic PPI use is associated with:
  - Clostridium difficile infection
  - Osteoporotic fractures
  - Community and hospital-acquired pneumonia
  - PPI therapy is expensive.

**AIM**

1) Raise awareness about over use of acid suppression therapy (AST).
2) Evaluate resident views on outpatient PPI usage and identify barriers to their discontinuation.
3) Analyze the effect of a PPI information sheet on prescribing habits.

**METHODS**

- 12 internal medicine residents surveyed about PPI usage in their continuity clinic.
- An pamphlet about PPI-related costs, side effects, and guidelines for use was written.
- Demographics for 201 patients visiting IU Health AACC before (6/2016 - 7/2016) and after (8/2016-9/2016) pamphlet distribution.
- Age, sex, acid suppression therapy (medication name, dose, frequency), etiology, prior EGD results, discontinuation of AST.
- Chi-squared analysis used to determine significance of the intervention.

**RESIDENT SURVEY RESULTS**

- 8% (1/12) re-evaluate PPI use each clinic
- 25% (3/12) believe patients on PPI for proper indication
- 92% (11/12) motivated to discontinue unwarranted PPI use
- 75% (9/12) feel uncomfortable discontinuing acid suppression therapy
- 58% (7/12) think guidelines are unclear

**DATA RESULTS**

- 201 total visits (92 male, 109 female)
- 93 pre- and 108 post-intervention
- 37.8% (76) on acid suppression therapy
- 36 pre-intervention, 40 post-intervention
- After information sheet distributed:
  - Significantly increased rate of AST discontinuation for eligible patients
  - 7.4% (2/27) vs 50% (16/32); $\chi^2 = 12.53; p<0.001$
  - Non-significant change in EGD referrals
  - 2.8% (1/36) vs 5% (2/40): $\chi^2 = 0.25; p = 0.619$

**CONCLUSIONS**

- PPIs are over-used in the outpatient setting.
- Physicians are uncomfortable discontinuing PPIs.
- Increasing awareness of PPI-related side effects, costs, and guideline-based use can decrease unwarranted PPI use.

**FUTURE DIRECTIONS**

- Discontinue automatic refills
- Add 8-week trial prescription on Cerner
- Collect data on relapse rates

**RESIDENT SURVEY RESULTS**

**Table 1. Cost of acid suppression therapy for 30 days**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Self-Pay</th>
<th>Branded List</th>
<th>Generic List</th>
<th>Medicare Part D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lansoprazole</td>
<td>30mg daily</td>
<td>$176.93</td>
<td>$25-40</td>
<td>$172.3</td>
<td>$17</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>300mg BID</td>
<td>NA</td>
<td>$15-20</td>
<td>$150.00</td>
<td>$150.00</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>800mg BID</td>
<td>NA</td>
<td>$15-20</td>
<td>$150.00</td>
<td>$150.00</td>
</tr>
</tbody>
</table>

**Figure 1. Information sheet**

**Figure 2. Patient characteristics**

**Upper GI Etiologies**

- GERD 67% (52)
- Other 19% (15)
- Acid Suppression Therapy
  - H2RA 16% (12)
  - PPI 84% (64)

**Lower GI Etiologies**

- Chronic PPI use is associated with:
  - GI bleed
  - Complicated Ulcers
  - Obesity
  - H. Pylori
  - Inflammation
  - Early symptoms
  - Weight loss

**Lifestyle Modifications**

- Smoking cessation, weight loss, family history
- Consider EGD
- Re-evaluate patient symptoms every clinic to determine if discontinuing therapy can be attempted.

**Drug**

- Lansoprazole, ranitidine, cimetidine

**Alarm Signs**

- Ulcer pain, vomiting, weight loss

**Complicated Ulcers**

- GI bleed
- Infection
- Perforation
- Complicated ulcer

**H. Pylori Treatment (1st Line)**

- Clarithromycin 500mg BID
- Pantoprazole 40mg BID
- 7-day course of PPI

**Community and hospital-acquired pneumonia**

- C. difficile infection

**H. Pylori Treatment (2nd Line)**

- Clarithromycin 500mg BID
- Metronidazole 500mg BID

**Figure 3. Patient characteristics**

**Table 2. Cost of acid suppression therapy for 30 days**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Self-Pay</th>
<th>Branded List</th>
<th>Generic List</th>
<th>Medicare Part D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>40mg daily</td>
<td>$129.01</td>
<td>$25-40</td>
<td>$15</td>
<td>$10 (tier 2)</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>40mg daily</td>
<td>$122.74</td>
<td>NA</td>
<td>$17</td>
<td>NA</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>30mg daily</td>
<td>$176.93</td>
<td>$25-40</td>
<td>$30-60</td>
<td>NA</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>40mg daily</td>
<td>$255.68</td>
<td>$25-40</td>
<td>NA</td>
<td>$29 (tier 3)</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>300mg BID</td>
<td>NA</td>
<td>$15-20</td>
<td>$4-10</td>
<td>$10 (Tier 2)</td>
</tr>
</tbody>
</table>

**FUTURE DIRECTIONS**

- Discontinue automatic refills
- Add 8-week trial prescription on Cerner
- Collect data on relapse rates

**Figure 4. Patient characteristics**

- If still symptomatic after 2 weeks on H2-blocker, restart PPI at lowest dose possible.
Fever in a Heart Transplant Patient: Don’t Forget the Tick
Anthony Wood MD, Andrew Wiele DO, Azam Hadi MD, Department of Medicine, Indiana University, Indianapolis, IN

Learning Objectives
• Recognize the clinical presentation of human monocytic ehrlichiosis (HME).
• Discuss the implications of delayed therapy.
• Investigate the relatively low incidence of HME in Indiana.

The Case
• A 49-year-old male with a h/o orthotopic heart transplantation four years prior (on tacrolimus and mycophenolate) presented with a six day history of fevers to 39 degrees Celsius, fatigue, nausea, vomiting, diarrhea, anorexia, and oliguria.
• Denied recent travel, sick contacts, rash, antibiotic use, and animal exposure.
• Vital signs WNL, and PE unremarkable.
• Smear showed minimal schistocytes, so plasmapheresis was initiated for treatment of possible TTP.

But upon further review...

What is Human Monocytic Ehrlichiosis?
• Tickborne, obligate intracellular bacterial infection of the Ehrlichia genus
• The lone star tick (Amblyomma Americanum) is the predominant tick vector with the white-tailed deer as the major host.

Implications of Delayed Therapy

Signs/Symptoms

<table>
<thead>
<tr>
<th>Signs/Symptoms</th>
<th>% (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>97 (833)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>57 (50)</td>
</tr>
<tr>
<td>Headache</td>
<td>40 (34)</td>
</tr>
<tr>
<td>Lassitude</td>
<td>22 (19)</td>
</tr>
<tr>
<td>Nausea</td>
<td>44 (39)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>33 (29)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22 (19)</td>
</tr>
<tr>
<td>Cough</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Rash</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Stiff neck</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Confusion</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Laboratory finding</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Elevated serum AST or ALT level</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

Diagnostic Tests

<table>
<thead>
<tr>
<th>Weeks after onset</th>
<th>Diagnostic test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EHRME</td>
</tr>
<tr>
<td>1</td>
<td>Blood smear evaluation</td>
</tr>
<tr>
<td></td>
<td>PCR</td>
</tr>
<tr>
<td></td>
<td>Serologic testing</td>
</tr>
<tr>
<td>2</td>
<td>PCR</td>
</tr>
<tr>
<td></td>
<td>Culture</td>
</tr>
<tr>
<td></td>
<td>Culture</td>
</tr>
</tbody>
</table>

Why is Incidence in Indiana so Low?

• Nationwide incidence has doubled in the past decade, and its tick vector continues to spread.

But only 4 cases of HME per million persons per year.

WHY?

Resolution
• Patient confirmed recent tick bite 2 weeks prior. Started on doxycycline with quick clinical recovery and discharged 3 days later.
• Ehrlichia Chaffeensis PCR and serology (IgM) positive.

Why is Incidence in Indiana so Low?

Indiana has ticks...

But only 4 cases of HME per million persons per year.

WHY?

Why is Incidence in Indiana so Low?

• Nationwide incidence has doubled in the past decade, and its tick vector continues to spread.

But only 4 cases of HME per million persons per year.

WHY?

References
• CDC. Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever and Other Spotted Fever Group Rickettsioses, Ehrlichioses, and Anaplasmosis — United States. MMWR Morb Mortal Wkly Rep 2016;65(2):1–44

Background

Serum folate levels are a commonly ordered study for macrocytic anemia during an inpatient stay. The United States has had a mandatory folic acid fortification since 1998, and since then folic acid deficiency rates have decreased. Several studies in the past have suggested that folic acid testing is an over utilized test in the inpatient setting.

Objective

Our objective was to determine to rate of deficiency, charge per test, cost per deficient result, and possible savings for inpatients with macrocytosis where serum folate was tested.

Methods

The electronic medical record at a large community hospital was reviewed for any incidence of folate testing that occurred in a patient that also had macrocytosis. 580 patient folate levels were tested between 1/1/2015 and 12/31/2015. Cost analysis was performed on a per patient basis.

Results

Between 1/1/2015 and 12/31/2015 there were 580 patient cases identified with macrocytosis in which folate testing was performed. Of these 580 tests, a total of 11 cases (1.9%) were found to be folate deficient (defined as <3.4ng/ml). Combined testing available at our institution for B12/folate has a cost basis of $224 per test, for a total of $129,920. B12 only testing for these 580 patients at a cost of $79 per test, would cost $45,820. These 11 folate deficient patients would cost an extra $2464. A step-wise diagnostic approach to our patient population would therefore provide a cost savings of $81,636 per year for our institution alone.

Conclusions

Since the mandatory fortification of folic acid in the United States began in 1998, the rate of folic acid deficiency has dropped dramatically. Therefore, in countries where folic acid fortification is required, folic acid testing in patients with macrocytosis has a low utility and is not cost effective. Significant cost savings can be found by taking a step-wise approach to the patient with macrocytosis. This is a very simple and easy to implement cost savings strategy for any hospital institution.

Bibliography

I Feel Like Something Bad Is About To Happen: A Case of a Pheochromocytoma

Mounish Karlapudi, MD¹, Ryan M. Johnston, MD², Indiana University Health Ball Memorial Hospital Internal Medicine Residency Program, Muncie, IN,

Abstract
A case of a 36-year-old female with a past medical history of anemia, anxiety, headache, and CVA presented with palpitations, neck pain, dizziness and headache without hypertension culminating in a diagnosis of pheochromocytoma.

Introduction
An anxious appearing obese African American female presented to the emergency department (ED) with a headache and a "weird feeling, like something bad was about to happen." She endorsed dyspnea, palpitations and a throbbing neck pain with nausea, vomiting, blurry vision, and generalized body tremors lasting 15 minutes.

She endorsed these events had been happening for 2 years, 4 – 5 times/day, prompting several ED visits in the past. The patient did not mention a previous diagnosis of hypertension. Prior to admission, the patient had undergone an extensive workup including an MRI demonstrating two small lacunar infarcts and an unremarkable stress test.

Vitals & Physical Exam
Upon initial presentation, the patient was not tachycardic. She was normotensive an EKG showing normal sinus rhythm with no ischemic changes.

Patient was not short of breath of diaphoretic. Cardiac examination showed a regular rate, rhythm, and no evidence of murmurs. Respiratory examination was unremarkable. Abdomen was soft, non-tender, and non-distended. Neurologic examination was intact without tremors.

Lab Studies

<table>
<thead>
<tr>
<th>Test</th>
<th>Value Found</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Normetanephrine</td>
<td>5.2 nmol/L</td>
<td>&lt;0.90 nmol/L</td>
</tr>
<tr>
<td>Plasma Metanephrine</td>
<td>1.7 nmol/L</td>
<td>&lt;0.50 nmol/L</td>
</tr>
<tr>
<td>Urine Normetanephrine:Cr</td>
<td>1297 mCg/gm Cr</td>
<td>60-216 mCg/gm Cr</td>
</tr>
<tr>
<td>Urine Metanephrine:Cr</td>
<td>954 mCg/gm Cr</td>
<td>29-158 mCg/gm Cr</td>
</tr>
<tr>
<td>Total Metanephrine:Cr</td>
<td>2251 mCg/gm Cr</td>
<td>106-316 mCg/gm Cr</td>
</tr>
</tbody>
</table>

Imaging
CT abdomen and pelvis showed a mass in the left adrenal gland approximately 3.1 x 2.5 x 2.9 cm.

Discussion
A pheochromocytoma is a rare neuroendocrine tumor with a peak incidence between the third and fifth decades of life. Classically, patients report headache, palpitations, diaphoresis, and are found to be hypertensive. Approximately 0.02% - 0.5% of patients are diagnosed with pheochromocytoma on hypertensive workup, whereas 10% of pheochromocytomas are found incidentally. In this case, the patient did not present with hypertension or tachycardia, although headaches and paroxysms of adrenergic symptoms were apparent.

The patient was started on alpha blockade therapy with prazosin. Beta-blockade was started 2 weeks later, and laparoscopic robot-assisted left adrenalectomy was scheduled.

A final pathologic diagnosis of pheochromocytoma was confirmed from a mass measuring 3.4 cm in greatest dimension. Sections of the tumor demonstrated a circumscribed hypercellular neoplasm with a predominantly nested architecture and consisting of epithelioid cells with stippled chromatin and inconspicuous nucleoli.

Past Medical History:
- Anemia
- CVA
- Headache
- Anxiety

Surgical History:
- None

Social History:
- ½ - 1 PPD tobacco smoker for 19 years

Family History:
- Mother has HTN.
- Father has diabetes.

It is important to be cognizant that this rare tumor can present with a myriad of symptoms. Some symptoms may not be classical, therefore it is important to not overlook the diagnosis of pheochromocytoma as the consequences could lead to a great deal of morbidity and mortality.

References

Acknowledgements
I would like to thank Dr. Samuel Kim for his assistance on this case.

I would like to thank Dr. Chandu Sundarum for accepting this case for surgery.
Orphan Drug Development: A Viable and Undervalued Research Opportunity

Hegwood, E.¹, Raddad, E.², Lancaster, J.², Persinger, C.², Shen, L.², Deeg, M.²

¹ Marian University College of Osteopathic Medicine (MU-COM) ² Eli Lilly & Co.

Importance

Industry as a whole continues to hold the perception that orphan disease treatment pursuits, those developed specifically for individuals with rare diseases, lack economic viability despite the medical need for their therapies. Traditionally, companies choose to employ large multi-phase studies when developing treatments for drug or device therapies and expend tremendous costs to bring therapies to market. To innovate, there has been some consideration of investment in tailored therapy trials. However, these clinical studies often attempt to break down complex disease states, such as diabetes, and have been unable to provide adequate valuation despite smaller research target due to the complexity of the disease states. As such, orphan targets provide an alternative to the current costly development landscape by helping us to understand disease states with less genomic diversity in order to evaluate methods of expedited drug development (Figure 1).

Figure 1. Drug development landscape

Objective

Our study first looked to evaluate and explore how a standardized orphan study development framework (archetype) might be represented. Then, it sought to evaluate how the economic impact (economic analysis) of such a framework differed from the traditional drug development pathway using historic industry ‘standards’ for comparison (provided in partnership with Eli Lilly & Co.). The main economic evaluation would be to calculate endpoints used in industry to determine viability for drug development, mainly determined by expected net present value (eNPV) of both cost and revenue parameters.

Assumptions

Given the complicated drug development landscape, baseline assumptions had to be considered to create an adequate orphan archetype model. The assumptions were as follows: the investor was external in origin, the drug indication was orphan exclusive (either for rare or ultra-rare diseases), candidate selection had clear value proposition, historical data was available for archetype development, and the design would be simple in design with standard value drivers.

Participants

Key eligibility and characteristics for use in orphan archetype modeling included drug or devices with an orphan exclusivity indication (marketed solely for orphan use), excluded oncology products, were either approved for chronic or acute disease treatments and classified as a treatment for either simple or complex disease states.

Materials & Methods

Baseline data was gathered from the public FDA approvals database retrospectively for the most recent 10 years on all orphan approvals. Economic analysis was then performed comparing the standardized orphan archetype to standardized historical pharmaceutical study model provided by industry.

Results

For the creation of the orphan archetype, 214 orphan approvals from the FDA database in the last 10 years were approved, 99 of which met our indication for study participation and were randomly sampled to show fractional representation in our study analysis. The archetype was averaged around this data and found to have around 144 participants per pivotal trial with an average of 288 participants needed for approval. FRD to FS (Phase III) averaged about 4 years. The majority of orphan approvals were found to be biologics that were for chronic and complex diseases in adult populations and approximately half had expedited review or development. The final orphan archetype developed from our data analysis, illustrated by study phase, is shown in Figure 2.

Figure 2. Final orphan archetype

Economic analysis demonstrated a weighted average cost of capital (WACC) value of 0.11, peak sales values of 581 million for the sample of orphan drugs, overall eNPV of $138 million and internal rate of return (IRR) of 18% with overall a significantly lower development cost. eNPV per year for development per year is shown in Figure 3.

Figure 3. Economic analysis of orphan archetype

Conclusions

Though further sensitivity analysis can be performed, this base case analysis suggests that orphan exclusive drug development is a viable option for investment. It has the potential to provide accelerated drug development with more than adequate investment returns. Given that the vast majority of these diseases still lack viable treatment modalities and the prevalence of orphan diseases is significant, these investments meet both an important medical imperative and need.

References

• Eli Lilly & Co. drug development standards
• FDA Orphan Approvals Database: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/
Inpatient Compliance with Current Guidelines for Frequency of Measuring Hemoglobin A1c
Audreem Singson, MD¹,
¹Indiana University Health Ball Memorial Hospital Muncie, IN

Objective
To measure inpatient compliance with current guidelines for frequency of A1c monitoring in patients with diabetes and to implement an improved compliance strategy.

Introduction
Type 2 diabetes is a rapidly growing chronic disease and a significant public health problem. The American Diabetes Association recommends routinely measuring hemoglobin A1c to monitor adequate control of diabetes. However, there is no benefit to checking A1c more frequently than every 90 days, which often occurs in the inpatient setting.

Study Population
Medical Diabetes Unit (MDU), and Medical Telemetry Unit (MTU)

Overview of Study Design
- Identify how A1c’s are being ordered on the MDU and MTU by Cerner single order chart audit
- A1c order may include the comment “If no Hgb A1c results in the last 90 days,” then make sure Lab Results time bar goes back far enough
- Right click the time bar to change time interval, for example to 1 year back
- Identify 100 charts with A1c performed April-July 2015 on the MDU and MTU with a previous A1c recorded in the chart
- Calculate the percent of A1c’s performed in less than 90 days

Methods
- Identify 100 charts with A1c performed in April-July 2015 on the MDU and MTU with a previous A1c recorded in the chart
- Calculate the percent of A1c’s performed in less than 90 days

Handout reviewed with nurse managers and nursing staff on the MDU and MTU:
- If Hgb A1c order has a comment to draw “If no Hgb A1c results in the last 90 days,” then make sure Lab Results time bar goes back far enough
- Right click the time bar to change time interval, for example to 1 year back

Results
Figure 1. 100 charts with A1c performed April-July 2015 and a previous A1c were identified, and 46% (n=100) A1c’s were performed in <90 days. After nursing educational intervention, 100 charts with A1c performed January-March 2016 and a previous A1c were identified, (n=100) A1c’s were performed in <90 days (p value not significant, 0.23).

Discussion
- Pre-checked lab orders can be useful in meeting quality measures, but there is also the risk of unnecessary lab testing and the associated cost
- A1c test costs $37.80 to perform and the mark-up price is $108.00
- The nursing educational intervention in this study did not result in a significant decrease in unnecessary A1c’s likely due to:
  1) most A1c orders do not include cancellation parameters
  2) pre-checked A1c in the Insulin SubQ Powerplan allows for unnecessary A1c’s to be performed too easily, despite the use of an order comment

Conclusion
The nursing educational intervention did not significantly decrease unnecessary A1c’s. A1c’s can be ordered within Powerplans or ordered separately, so removing pre-checked A1c from Insulin SubQ Powerplan and notifying providers if an A1c has already been ordered or performed in less than 90 days may be effective in reducing unnecessary A1c’s.

References
Learning Objectives
- Consider that Clopidogrel requires first pass metabolism to achieve active form
- Recognize that a substantial proportion of the population has a mutation of the enzyme responsible for activation

Patient Presentation
A 92-year-old Caucasian male with a history of hypertension presented to our hospital with confusion and transient expressive aphasia.
- Patient diagnosed with a TIA.
- Patient started on Clopidogrel and genetically tested for CYP2C19 genotype.
- Found to be a heterozygote, with one loss of function allele.
- P2Y_{12} assay showed no platelet inhibition.
- Patient switched to Aspirin – Dipyridamole (Aggrenox) for stroke prevention.
- Patient is doing well on Aggrenox.

Evidence-Based Management
The literature is full of case studies, analyses, and trials regarding Clopidogrel metabolism. Multiple studies including MATCH, CAPRIE, ESPRIT, and PReFESS guided our clinical management in this case. Interestingly, despite a single allele mutation, the patient had no response to Clopidogrel whatsoever, putting him at higher risk of stroke.
- There are viable, cost-effective means of identifying at-risk patients:
  - Genetic testing (Cheek swab / PCR).
  - P2Y_{12} assay (VerifyNow™).
  - Equally efficacious alternative therapies exist for stroke prevention.

Discussion
This case demonstrates the possibility of treatment failure in patients who do not respond to Clopidogrel. The lack of efficacy is due to a fairly common mutation of the CYP2C19 gene, which prevents Clopidogrel from achieving its active form in vivo.
- 30% of the population may carry a loss of function allele.
- Many factors determine Clopidogrel response in vivo:
  - Absorption
  - Drug interactions
  - Several genetic polymorphisms that are not as commonly tested as the CYP2C19 allele
- Based on the literature, patients with single allele mutations should still have some enzyme function; however, our patient does not.
- Some studies show potential cost effectiveness of testing.
- Recognizing the potential for treatment failure has the potential to substantially improve outcomes.
- We have other options that do not require first pass metabolism.
- Why not check platelet function?

References

Reproduced with Permission. Simon et al. © NEJM 2009
INTRODUCTION
Common variable immune deficiency (CVID) is a primary immune disorder characterized by hypogammaglobulinemia. It is mostly diagnosed in teenagers with an estimated life expectancy into the fourth decade of life, with regular IVIG infusions.

Diagnosis in adult patients over 40 can be missed.

HISTORY OF PRESENT ILLNESS
A 43 year old man with a history of bronchiectasis presented with sepsis and acute hypoxic respiratory failure secondary to a left upper lobe pneumonia. His history was notable for:
- Frequent bacterial pneumonias since the age of 19
- Four hospitalizations within the past year for pneumonia

He was told that his bronchiectasis was due to excessive smoking but he had quit smoking 3 years prior.

LABORATORY DATA
CBC with differential at admission
- WBC: 18.8 (3.8-10.6)
- Absolute lymphocytes: 0.0 (0.8-3.65)
- Bands: 1.0 (0.9-8.0)

Immunoglobulins
- Serum IgM: <5 (0.7-14 mg/dL)
- Serum IgA: <20 (10-300 mg/dL)
- Serum IgG: <100 (400-1820 mg/dL)
- Subclass 1: <147 (382-929 mg/dL)
- Subclass 2: <20 (241-700 mg/dL)
- Subclass 3: <6 (22-178 mg/dL)
- Subclass 4: <3 (4-86 mg/dL)

Results within normal limits
- HIV by PCR and log 10, Alpha-1 antitrypsin, Urine Legionella and Streptococcus pneumoniae
- Post-vaccination titer
- Tetanus and pneumococcal: undetectable

IMAGING
CTA of the chest: bulky mediastinal lymphadenopathy, worrisome for a neoplastic process (Figure 1). Persistent bilateral tree-in-bud nodular opacities and lower lobe predominant bronchiectasis.

DIAGNOSIS
Diagnosis is made based on criteria laid out by the European Society for Immunodeficiencies and the Pan-American Group for Immunodeficiency.
- Marked decrease of serum IgG levels (<4.5 mg/dL) and a marked decreased below the lower limit in at least one of the isotypes IgM or IgA
- At least 4 years of age or older
- Lack of antibody immune response to polysaccharide and protein antigens from previous immunizations

DIAGNOSIS
Diagnosis is chiefly by exclusion of alternative causes of hypogammaglobulinemia.

OTHER INVESTIGATIONS
- Bone marrow biopsy: normocellular with trilineage hematopoiesis and no definitive evidence of malignancy.
- Flexible bronchoscopy and mediastinoscopy with lymph node sampling: Non-necrotizing, non-suppurative granulomatous lymphadenitis. Acid fast bacilli and Grocott's methenamine silver stains are negative for microorganisms.
- Flow Cytometry of lymph node sample: No aberrant immunophenotypic finding including a monoclonal B cell proliferation is identified.

IMAGING
- CTA of the chest demonstrates mediastinal lymphadenopathy concerning for a neoplastic process. Lymph node sampling is essential to evaluate for granulomatous and malignant disease.

MONITORING PATIENTS OVER TIME
CVID is a heterogeneous disease associated with a plethora of clinical features, as demonstrated in Figure 2 and Table 1a. Patients are at increased risk for malignancies, particularly Non-Hodgkin lymphoma (Table 1b).

ACKNOWLEDGEMENTS:
A special thank you to the St. Vincent Internal Medicine Medical Education program for supporting our presentation of this interesting case. Additionally, we appreciate the feedback and expertise of our colleagues who were involved in the care of this patient.

REFERENCES

LESSONS LEARNED
- The rare incidence and high clinical variability of CVID can present as a diagnostic challenge.
- There is no specific test for diagnosing CVID; so diagnosis is made by excluding similar conditions.
- Remember to maintain a broad differential diagnosis, take a thorough history, and systematically assess the patient’s immunological status.

CVID is an important diagnosis to make correctly as it requires serial IVIG infusions to reduce the risk for sepsis and close monitoring for complications, including malignant and autoimmune processes.
INTRODUCTION

Human monocytic ehrlichiosis (HME) is a potentially fatal, emerging infection spread through the bites of the Lone Star tick, Amblyomma americanum. As a rare infectious disease in Indiana, diagnosis is not well understood by most clinicians and may be missed, delaying treatment until after severe complications have occurred. In the absence of an apparent history for tick exposure, this can easily occur.

HISTORY OF PRESENT ILLNESS

A 74 year old man with minimal medical problems presented to our hospital with a headache. Five days ago, he visited an urgent care clinic obtain treatment for his headache and be evaluated for dysuria. He was subsequently treated for a urinary tract infection with resolution of symptoms, but his headache persisted. Aside from the headache, his only complaint was nausea. He did not have any respiratory or abdominal complaints, atheralgia, rashes, or constitutional symptoms.

Upon further questioning, it was revealed that he had been cleaning out his cabin in southern Indiana and had been bitten by several ticks.

PHYSICAL EXAM

Multiple ticks were found attached to his skin, were removed, and sent to the lab for further evaluation. The rest of the physical exam did not contribute to the diagnosis.

LABORATORY VALUES

Only abnormal values are reported below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count</td>
<td></td>
</tr>
<tr>
<td>White blood cell</td>
<td>11.1</td>
</tr>
<tr>
<td>Red blood cell</td>
<td>4.08</td>
</tr>
<tr>
<td>Platelet count</td>
<td>4650</td>
</tr>
<tr>
<td>Absolute neutrophil</td>
<td>0.4</td>
</tr>
<tr>
<td>Absolute lymphocyte</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Comprehensive metabolic panel

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>1.57</td>
</tr>
<tr>
<td>Aspartate aminotransferase</td>
<td>141</td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>74</td>
</tr>
</tbody>
</table>

At admission, IgM and IgG antibody testing for tickborne illnesses were negative for:

- Borrelia burgdorferi
- Ehrlichia chaffeensis
- Rickettsia rickettsii

Peripheral blood smear: Pancytopenia with occasional atypical lymphoid cells. No blasts seen.

Further workup was unrevealing, as the following results were within normal limits:

- Erythrocyte sedimentation rate
- Thyroid stimulating hormone
- Creatine phosphokinase
- HIV by PCR and log 10
- EBV and CMV (Qualitative RT-PCR, Antibodies IgM and IgG)
- CCP Antibody IgG

IMAGING AND OTHER STUDIES

MRI and CT of the Head with and without contrast: Within normal limits

- Chest X-Ray: Ribasilar infiltrates left greater than right.
- Chest CT with and without contrast: Bilateral pleural effusions and mild interstitial edema at the lung bases. No evidence of pneumonia.

Given that he did not have any mental status changes or acute neurological deficits, we did not perform a lumbar puncture since his pancytopenia placed him at a high risk for bleeding and infection.

Despite a negative workup, we empirically started him on doxycycline. He was expected to complete a 10 day regimen.

DIAGNOSIS

Four days after the original ehrlichiosis panel, repeat serologies with an immunofluorescence assay demonstrated E. chaffeensis positive IgM. The ticks originally sent for further evaluation were identified as A. americanum.

Laboratory criteria for diagnosis of HME:

- Demonstration of a 4-fold change in antibody titer to E. chaffeensis antigen by IFA in paired serum samples, or
- Positive PCR assay and confirmation of E. chaffeensis DNA, or
- Identification of morulae in leukocytes and a positive IFA titer to E. chaffeensis antigen, or
- Culture of E. chaffeensis from a clinical specimen

OUTCOME

Doxycycline is the treatment of choice for tickborne diseases. With this treatment, his headache subsided and his laboratory findings also began to recover. He remained on this antibiotic for 10 days with complete resolution of his symptoms.

LESSONS LEARNED

If left untreated, severe cases of HME can result in respiratory and renal failure, coagulopathy resulting in gastrointestinal bleeding and neurological abnormalities from infection of the brain and spinal cord. The estimated case fatality rate is estimated at 1.8% and early antibiotics are curative. Therefore, a high clinical suspicion with a negative diagnostic workup should not delay treatment.

ACKNOWLEDGEMENTS: A special thank you to the St. Vincent Internal Medicine Medical Education program for supporting our presentation of this interesting case. Additionally, we appreciate the feedback and expertise of our colleagues who were involved in the care of this patient.
INTRODUCTION

Heroin overdose constitutes over 20% of all emergency department visits related to drug misuse or abuse. Since 2000, the number of deaths related to drug overdose has increased 137%, including a 200% increase in the number of deaths involving opioids. Because heroin can only be detected on urine drug screen for up to 48 hours, clinical presentation is important for diagnosis.

Non-cardiogenic pulmonary edema has been attributed to heroin injection, while inhalation of heroin has been associated with acute interstitial pneumonia presenting as hypoxia and frothy, pink-tinged pulmonary secretions. We present a case of heroin inhalation resulting in alveolar hemorrhage in an otherwise clinically stable patient.

CASE DESCRIPTION

A healthy 19-year old male was transferred to our hospital with hematemesis, hemoptysis, and epistaxis. He reported shortness of breath, persistent cough, and chills. Upon admission to the outside hospital, vitals were stable and physical exam was positive for course rhonchi of the right lung field.

LABORATORY DATA

The following laboratory values were obtained on initial presentation.

<table>
<thead>
<tr>
<th>Value Type</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>39.8°C</td>
</tr>
<tr>
<td>White Blood Cells</td>
<td>15,000</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>12.0 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>250,000</td>
</tr>
<tr>
<td>Blood Urea Nitrogen</td>
<td>14.0 mg/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.8 mg/dL</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.9 g/dL</td>
</tr>
<tr>
<td>Sodium</td>
<td>140 mEq/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.9 mEq/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>100 mEq/L</td>
</tr>
<tr>
<td>Glucose</td>
<td>127 mg/dL</td>
</tr>
</tbody>
</table>

IMAGING

Figure 1: PA chest x-ray demonstrating diffuse alveolar process – pneumonic infiltrate vs. intrapulmonary hemorrhage.

Figure 2: CT scan (anteroposterior view) demonstrating diffuse right lung patchy opacities, concerning for alveolar hemorrhage.

Figure 3: CT scan (axial view) demonstrating diffuse right lung patchy opacities, concerning for alveolar hemorrhage.

DIAGNOSIS

Given the unusual presentation of alveolar hemorrhage isolated to two lobes, further history-taking revealed that the patient had inhaled heroin 2 days prior to the onset of symptoms. Pulmonary consultation confirmed our diagnosis of alveolar hemorrhage secondary to heroin inhalation. The patient was managed conservatively with resolution of his symptoms 4 days after heroin inhalation.

CONCLUSION

Heroin inhalation is infrequently reported in the literature, and when reported, typically presents as acute interstitial pneumonia. Our patient demonstrates a unique presentation of heroin inhalation overdose. Initially, he did not admit to heroin use, so we were unsure of what was causing his epistaxis, hemoptysis, and hematemesis and if they were all related. After admission, it was determined that the bleeding began in his nose due to irritation from the inhalation of heroin. This then resulted in blood entering the GI tract, causing hematemesis. Moreover, the inhalation of heroin caused a chemical pneumonitis with alveolar hemorrhage and hemoptysis. To our knowledge, this is the first reported case of alveolar hemorrhage due to heroin inhalation.

REFERENCES


Acute Pancreatitis with Normal Lipase

W. Wyatt Wilson, MSPH, Karen Wolf, MD
Department of Internal Medicine
Indiana University School of Medicine, Indianapolis, Indiana

Learning Objectives
- Recognize the diagnosis of acute pancreatitis in both typical and atypical presentations
- Recognize the presentation of acute pancreatitis with a normal serum lipase
- Understand the management of hypertriglyceridemia-induced pancreatitis (HTAP)

Introduction

Acute pancreatitis is diagnosed with two of the following three findings:
1. Acute onset of persistent, severe epigastric pain radiating to the back
2. Serum lipase elevated three times the upper limit of normal
3. Radiographic findings consistent with acute pancreatitis on CT, MRI or transabdominal US [1]

- Serum lipase has a reported sensitivity and NPV ranging 94-100% in the setting of acute pancreatitis, often negating the need for any further diagnostic imaging when patient’s present with epigastric pain

Case Description

HPI: A 30-year-old female with panhypopituitarism from necrosis due to a documented abscess, insulin-dependent type II diabetes mellitus, and one previous episode of pancreatitis presented to an outside hospital with acute onset epigastric pain and nausea. She denied fever, myalgias, sick contacts, emesis, dysuria, alcohol use, gallstone, new medications or new exotic foods as well as any chest pain, shortness of breath, or changes to bowels or bladders habits.

Past Medical Hx: Adrenal insufficiency, constipation, hypertriglyceridemia

Meds: Gemfibrozil, levothyroxine, hydrocortisone, DDVAP, medroxyprogesterone, metoclopramide, insulin glargine, insulin glulisine

Past Family Hx: HTN, HLD

Past Surgical Hx: C-section

Social Hx: never smoker, alcohol, or drug use

Physical Exam
- Vitals: 37.5F, 95/50, HR 101, RR 15, SpO2 98% on 3LNC
- General: NAD, diaphoretic
- HEENT: dry mucosa, EOMI, O/P clear w/o exudates, petechiae or erythema
- Cardio: increased rate, RR, no m/r/g, no JVD, no peripheral edema
- Lung: clear to auscultation bilaterally
- GI: decreased BS, diffuse tenderness without rebound or guarding
- Neuro: AAOx3, CN II-XII intact without focal abnormalities, speech organized
- MSK: no joint or muscle tenderness or effusions; skin warm and dry

Data
- CBC: 10.7 WBC, 11.1 Hgb, 176 Pitt
- Anion Gap: 7
- TG: 3,128
- CMP: 132 Na, 8.0K, 15HC03, >700Glc
- Lipase: 129
- Lactate: 2.9
- Ca: 7.0
- ABG: 7.27 / 28 / 108 / 98%

Imaging
- CT abdomen w/ contrast: edema along the retrocrural mesenteric space without abscess, necrosis calcification or pseudocyst and bibasilar atelectasis.
- CXR: no cardiopulmonary abnormality

Hospital Course
- She was transferred to the MICU and was managed initially with:
  - D51/2NS for fluid-responsive hypotension and correction of hyponatremia
  - Hydromorphone for analgesia
  - Insulin drip to correct hyperglycemia and ketoacidosis
  - In combination with her insulin drip, she was restarted on home gemfibrozil, begun on prophylactic/therapeutic heparin to correct her hypertriglyceridemia.
  - Also restarted on home levothyroxine, hydrocortisone and DDVAP, careful to avoid worsened hyponatremia in the setting of pancreatitis.

Insulin drip was transitioned to subcutaneous once triglycerides were below 500. She was weaned from nasal cannula, transitioned to oral pain medication and transferred out in stable conditions with eventual resolution of lactic acidosis.

Table 1. Values of serum lipase in the diagnosis of acute pancreatitis [2]

<table>
<thead>
<tr>
<th></th>
<th># of patients</th>
<th>Sens %</th>
<th>Spec %</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kylanpa-Back, 2002</td>
<td>237</td>
<td>55</td>
<td>99</td>
<td>88</td>
<td>94</td>
</tr>
<tr>
<td>Treacy, 2001</td>
<td>328</td>
<td>67</td>
<td>97</td>
<td>80</td>
<td>94</td>
</tr>
<tr>
<td>Gumaste, 1993</td>
<td>170</td>
<td>100</td>
<td>99</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>Pantechni, 1989</td>
<td>54</td>
<td>100</td>
<td>81</td>
<td>93</td>
<td>100</td>
</tr>
<tr>
<td>Hemingway, 1988</td>
<td>20</td>
<td>100</td>
<td>96</td>
<td>95</td>
<td>100</td>
</tr>
<tr>
<td>Steinberg, 1985</td>
<td>216</td>
<td>87</td>
<td>99</td>
<td>95</td>
<td>97</td>
</tr>
</tbody>
</table>

Discussion

Despite a normal lipase, the patient’s work up qualifies for a diagnosis of acute pancreatitis. To date, there are only a handful of reports of acute pancreatitis with normal serum lipase levels.

In a normal functioning pancreas with acute inflammation, lipase levels rise 4 to 8 hours after inflammation, peaking at 24 hours, normalizing by 14 days. Given its high sensitivity, normal serum lipase is commonly used to rule out disease. Common etiologies for altered serum lipase exist. Levels can be falsely elevated in intra-abdominal infections or from poor renal clearance. Serum lipase can also be falsely normal in acute on chronic pancreatitis from excocrine gland destruction.

In the setting of HTAP, serum amylase and lipase can also be falsely low. While assay interference has been established with falsely normal serum amylase levels, this has not been reported for low lipase levels. Indeed, the radiographic evidence disqualifies our patient from acute on chronic pancreatitis. The mechanism for low lipase in this setting is poorly understood.

HTAP (>1,000 mg/DL) should be suspected with poorly controlled DM (particularly T2), an underlying familial hyperlipidemia and the absence of more common etiologies (EtOH, gallstones). The exact mechanism is not yet understood. It is managed with fluid resuscitation, analgesia and continuous insulin infusion and heparin, which stimulates lipoprotein lipase (LPL) thereby decreasing TG present on VLDL [3]. Apheresis, which removes available TG and chylomicrons, has shown promising preliminary data but is not yet a mainstay of treatment.

References

A Case of Primary Central Nervous System Lymphoma with Systemic Metastasis Involving the Ovaries

Sarah M. Jeong, MD, Mohammad Sami Bakdash, MD, Darryl G. Morrical, MD, William B. Fisher, MD
Indiana University Health Ball Memorial Hospital, Muncie, IN

Introduction

- Primary central nervous system lymphoma (PCNSL) is a rare disease affecting the neuraxis that accounts for less than 5% of non-Hodgkin’s lymphomas (NHL) and 1-3% of all central nervous system (CNS) malignancies.

- While systemic lymphoma is known to metastasize to the brain and leptomeninges, PCNSL is characterized by its confinement to the nervous system.

- However, systemic dissemination occurs in extracranial sites in 7-10% of cases, with documented involvement in the kidney, skin, and testis.

- Here, we report a case of PCNSL with histologically confirmed systemic metastasis to the lungs and clinical evidence of metastasis to the bilateral ovaries.

Methods & Materials

- A comprehensive review of PCNSL case reports in the medical literature.

- A review of the molecular pathogenesis as well as histochcmical and molecular characteristics of PCNSL.

- A comprehensive review of the patient’s chart.

Case Chronology

- **2013**
  - Pt presents to the ED complaining of headache, difficulty judging distances, and right leg weakness
  - MRI head shows 6-8cm mass-like lesion in the left parietal lobe, as shown in Figure 1
  - Stereotactic biopsy reveals diffuse large B-cell lymphoma

- **2013-2014**
  - Pt receives 12 cycles of methotrexate, 4 cycles of rituximab, 2 cycles of cytarabine
  - Pt attained complete remission as documented on serial MRIs, last documented in 7/2016

- **8/2016**
  - Pt presents to the ED with worsening dyspnea and was found to have a large left-sided pleural effusion with mediastinal lymphadenopathy on CT chest
  - Thoracentesis revealed exudative fluid containing diffuse large B-lymphocytes on histology, with a monoclonal population based on flow cytometry
  - CT abdomen showed bilateral adnexal masses with numerous enlarged pelvic and retroperitoneal lymph nodes, as shown in Figure 2
  - CA125 was elevated at 356.3 units/mL

- **9/2016 - Present**
  - CT scans show dramatic shrinkage of her lymphadenopathy and adnexal masses after 3 cycles of R-CHOP, as shown in Figure 3

Discussion

- PCNSL has been characteristically associated with immunodeficient patients, however the incidence in immunocompetent populations is increasing.

- Methotrexate-based chemotherapy is part of the first-line treatment for PCNSL. However, the prognosis of PCNSL remains poor compared to other extranodal lymphomas.

- Approximately 35-60% of PCNSL patients who have achieved complete remission experience recurrence within two years of diagnosis.

- Patients that experience recurrence of PCNSL demonstrate an overall survival of 8-18 months. At present, there is no standard treatment for recurrent PCNSL.

- PCNSL recurrence in extracranial sites is extremely rare, however there have been documented cases of metastasis to the kidney, skin, and testis

- To date, there has been no documented case of PCNSL relapse in the ovaries.

Conclusion

- Physicians should consider the possibility that ovarian masses do not always signify cancer of ovarian origin, even with an elevated CA125.

- Clinicians caring for PCNSL patients must be alert to the possibility of systemic metastasis, especially as local control of PCNSL improves.

References


Perplexing Palsy: A Case of Pachymeningitis

Daniel A. Stegelman, MD, Erick Christensen, MD, MPH
Indiana University Health Ball Memorial Hospital, Muncie, Indiana

Abstract

Introduction: Idiopathic hypertrophic pachymeningitis (IHM) is an uncommon condition with many possible etiologies including autoimmune diseases, neoplasms, and infections. The process involves a diffuse inflammation and thickening of the dura mater. Associated symptoms can include headache, nausea, and multiple nerve palsies. This disorder can be insidious in onset and occasionally masquerades as other more common encephalopathies.

Case Report: A 36-year old Caucasian female was admitted after she had been found lying on the floor for three days. Medical history included alcoholism, drug abuse, and multiple suicide attempts. She was intubated and given vasopressors for hypotension. She was febrile, tachycardic, and had diffuse wheezing. Differential diagnoses included severe sepsis, drug overdose, spousal abuse and neglect. Ethanol, urine drug screen, and blood cultures were negative. There were also no severe electrolyte derangements. Multiple head CTs showed no concerning findings.

When patient was extubated she was delirious and agitated, but able to follow simple commands. Once sedation wore off, it became apparent she had upper extremities weakness and was unable to move her legs. MRIs of the head and spine showed diffuse meningeal thickening surrounding the brain and spinal parenchyma with subsequent spinal cord compression. CSF protein was elevated. Other CSF studies including Syphilis IgG, VDRL, HSV1 and 2, West Nile, and CSF cultures were all negative. T-SPOT and ANA were also negative. Urine and blood Histoplasma antigens showed no reactivity. Elevated serum ACE level was also noted. Other CSF studies including Syphilis IgG, VDRL, HSV1 and 2, West Nile, and CSF cultures were all negative. T-SPOT and ANA were also negative. Urine and blood Histoplasma antigens showed no reactivity. CNS sarcoid was considered after discovering an elevated serum ACE level.

The patient remained febrile and had leukocytosis. She regained motor movement and was able to speak. She was delirious and agitated, but able to follow simple commands. MRI findings were characteristic and help distinguish it from other encephalopathies including infectious, neoplastic, and neurologic diseases.

Discussion: This case report demonstrates how pachymeningitis can be mistaken for other more common causes of encephalopathy. Although pachymeningitis is a rare disorder, its MRI findings are characteristic and help distinguish it from other encephalopathies. Biopsy specimens can be diagnostic but may not demonstrate inflammatory changes. Literature search of pachymeningitis case reports have shown improvement of symptoms with steroids indicating an inflammatory etiology. Diagnosis is made by ruling out other granulomatous and infectious diseases.

Conclusions

- IHM is associated with multiple neurologic presentations, with headache and cranial nerve palsies being the most common.
- This disorder can be insidious in onset and occasionally masquerades as other more common causes of encephalopathies including sepsis and drug overdose.
- IHM is best identified by MRI and the diagnosis is based on exclusion of other diagnoses including infectious, granulomatous, and inflammatory processes.
- MRI can show localized or diffuse dural thickening.
- Dural biopsies often show fibrosis and inflammatory cells in lymphocytes, although biopsies can show non-specific inflammatory changes.
- IHM is notable for its response to steroids and immunomodulating drugs which indicate its inflammatory nature.
- Disease Processes Known to be Associated with Pachymeningitis:
  - Tuberculosis
  - Syphilis
  - Primary Malignancy of the Meninges
  - Dural Metastases
  - Systemic Lupus Erythematosus
  - Granulomatosis with Polyangitis
  - Bechet's Syndrome
  - Sjogren's Syndrome
  - Takayasu's Arteritis

References

The Apple of My GI: A Rare Case of Isolated Intestinal Amyloidosis

Samantha Armstrong, M.D. , Rafat Abonour M.D.
Indiana University School of Medicine, Indianapolis, Indiana

BACKGROUND

Amyloidosis refers to a group of diseases where the primary pathological finding is extracellular deposition of insoluble, misfolded, polymeric protein fibers in tissues and organs.

- There are six types of amyloidosis, including primary (AL) amyloidosis, which is associated with monoclonal light chains in serum and/or urine and secondary (AA) amyloidosis which is associated with inflammatory, infectious and neoplastic diseases (1).
- Diagnosis of amyloidosis requires high clinical suspicion, abdominal fat pad aspiration, bone marrow biopsy or ultimately a biopsy of the affected organ.
- Histologically, a Congo Red stain visualizes the amyloid protein as “apple-green” birefringence in polarized light.
- If deposits are seen, typing of the amyloid is done with light chain immunohistochemistry, biopsy or ultimately a biopsy of the affected organ.
- Amyloid deposits are commonly seen in the heart and kidneys, but can affect any organ, tissue or nerve.
- Presenting symptoms are due to the amyloid deposits in the organ causing renal failure, heart failure, liver failure or nerve damage.

A 69-year-old Caucasian female with medical history significant for IgA Lambda Monoclonal Gammapathy of Undetermined Significance, complicated by proteinuria, presented with chief complaint of left lower quadrant pain. Associated symptoms included nausea, non-bilious, non-bloody emesis, early satiety, alternating complaints of diarrhea and constipation. Vital signs, physical exam and initial labs were unremarkable. She was admitted for dysmotility disorder evaluation.

- CT of the abdomen and pelvis was significant for wall thickening of the transverse colon.
- Esophagogram showed esophageal dysmotility with a weak peristaltic wave, as evidence by persistent contrast within the esophagus despite multiple dry swallows.
- Gastric emptying study showed significant delayed emptying
- Endoscopy demonstrated a normal appearing duodenum and colonic mucosa with architectural distortion. Biopsies of the esophagus, stomach and duodenum were taken; pathology exhibited positive congo red deposition. Colon biopsies were negative for amyloid.
- Bone marrow biopsy showed an infiltration with lymphoplasmacytic lymphocytes of 5% to 10%. Congo red negative and restricted for IgA. Further studies showed CD20 positive cells.
- The complete evaluation showed the diagnosis of primary (AL) intestinal amyloidosis without other organ involvement.

The patient was initially treated with a regimen including bortezomib/cyclophosphamide with minimal response. Given patient's CD20 positive cells, she was then treated with rituximab/cyclophosphamide/prednisone. To date, her amyloid markers are within normal limits. Despite this, she continues to suffer from impaired peristalsis that is symptomatically treated with erythromycin.

Pathology

Primary (AL) Amyloidosis

Secondary (AA) Amyloidosis

GI Amyloidosis

Gastrointestinal Manometry

Amyloidosis refers to a group of diseases where the amyloid protein accumulates in various tissues and organs due to the body’s inability to degrade or recycle it properly. This can result in organ damage and dysfunction. In patients with primary AL amyloidosis, the amyloid protein is produced by plasma cells, while in secondary AA amyloidosis, it is produced in response to chronic inflammation or infection.

Table 1: Comparison of Primary and Secondary GI Amyloidosis

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Primary (AL) Amyloidosis</th>
<th>Secondary (AA) Amyloidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes</td>
<td>Idiopathy and plasma cell dyscrasias</td>
<td>Chronic inflammatory disorders and infections</td>
</tr>
<tr>
<td>Deposits</td>
<td>Monoclonal immunoglobulin light chains, subcutaneous and muscular amyloidosis</td>
<td>Serum amyloid A protein, The pseudo membrane</td>
</tr>
<tr>
<td>GI symptoms</td>
<td>Constipation, mechanical obstruction and chronic intestinal pseudodiverticulosis</td>
<td>Diarrhea, malabsorption and weight loss</td>
</tr>
</tbody>
</table>

REFERENCES


8. Lymphoma
Retroperitoneal Paraganglioma Manifesting as Partial Duodenal Obstruction

Gabriel Kousourou MS4, Amanda Day MS4, Kapil Mehta M.D. FACP, St. Vincent Hospital, Department of Internal Medicine, Indianapolis, IN

Introduction

Pheochromocytomas are rare catecholamine secreting tumors located in the adrenal medulla that occur at a rate of 2-4 per million people a year. Within this population lies a small subset of individuals with extra-adrenal tumors, known as paragangliomas. Paragangliomas make up 10-18% of all pheochromocytomas and are derived from neural crest chromaffin cells.

Clinically, pheochromocytomas and paragangliomas often present with severe headache, diaphoresis and palpitations in the setting of persistent or episodic hypertension. While these signs and symptoms are most common, these tumors can also present in unusual ways such as psychosis, seizures and strokes. These clinical manifestations along with the propensity to induce fatal cardiac arrhythmias, hypertensive crisis, and death make identification of these tumors at an early stage imperative.

History of Present Illness

A 42-year-old Caucasian female with no past medical history began experiencing episodic hypertension, palpitations, headaches and “panic attacks” in 2012. These episodes reached as high as systolic 280 mmHg. In June 2015, she placed on amlodipine and atenolol. Six months later in January 2016, clonidine and spironolactone were added due to her abdominal pain and severe hypertension. Each time a new CT scan was performed showing no residual or recurrent mass and no clear explanation for her abdominal pain.

Case Resolution

• She was started on phenoxybenzamine and a beta blocker for blood pressure control.
• After appropriate medical management the patient underwent a robotic assisted laparoscopic excision of the paraganglioma.
• The final pathological results showed Zellballen clusters, which are classic morphological features of a paraganglioma.
• Genetic testing results for hereditary endocrine cancers and neurofibromatosis were negative.
• Since discharge, the patient has presented on multiple occasions to the emergency department with severe abdominal pain. Each time a new CT scan was performed showing no residual or recurrent mass and no clear explanation for her abdominal pain.

Discussion

• 1 in 3 adults in America have hypertension, the majority of which is essential.
• Secondary hypertension is responsible for 5-10% of all hypertension.
• Pheochromocytomas make up 0.5% of secondary hypertension.
• The preferential elevation of normetanephrine is specific to extra-adrenal pheochromocytomas as PNMT, the enzyme that catalyzes the conversion of norepinephrine to epinephrine is primarily located in the adrenal medulla.
• 10-50% of paragangliomas are hereditary and are associated with von Hippel-Lindau disease, Neurofibromatosis Type 1, familial paraganglioma, RET oncogene and Multiple Endocrine Neoplasia Type 2. This fact stresses the importance of genetic testing.
• 17% of pheochromocytomas and paragangliomas are metastatic.
• Currently there are no histologic markers that exist to determine whether the tumor is malignant or benign.
• The most common locations of metastasis are lymph ganglia, bones, liver and lungs.
• Surgical resection is curative for pheochromocytoma and paraganglioma. Treatment prior to surgery includes: alpha-adrenergic blockade, volume repletion and high salt diet for 7-14 days, followed by a beta-blockade three days before surgery. These measures are taken to prevent complications from intraoperative catecholamine surges.
• A right paraganglioma is 11.2 times more likely to recur compared to left.

Table 1: Plasma free metanephrines and urine metanephrines results from pheochromocytoma work-up.

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Pre-surgery</th>
<th>Post Surgery</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Metanephrine</td>
<td>737</td>
<td>180</td>
<td>≤205 μg/mL</td>
</tr>
<tr>
<td>Normetanephrine</td>
<td>681</td>
<td>126</td>
<td>≤148 μg/mL</td>
</tr>
<tr>
<td>Metanephrine</td>
<td>56</td>
<td>54</td>
<td>≤57 μg/mL</td>
</tr>
<tr>
<td>Urine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Metanephrine</td>
<td>1153</td>
<td>742</td>
<td>182-739 μg</td>
</tr>
<tr>
<td>Normetanephrine</td>
<td>984</td>
<td>560</td>
<td>88-649 μg</td>
</tr>
<tr>
<td>Metanephrine</td>
<td>169</td>
<td>182</td>
<td>58-203 μg</td>
</tr>
</tbody>
</table>

References

7. University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina.
Eliminating Waste:  
A Quality Improvement Project to Curtail the Overuse of Inpatient Cardiac Monitoring

1 Identification of Problem

Every day in every hospital in the country, strategies are being devised to use medical resources appropriately and to cut healthcare costs. One resource that is overused in the inpatient hospital setting is telemetry. The American Heart Association (AHA) established guidelines for the appropriate indications for telemetry, yet too often these criteria are not utilized by prescribing physicians. Several hospital systems across the nation have implemented telemetry ordering initiatives which have led to improved patient outcomes and significantly reduced costs.

The goal of this project was to see if a resident-led quality improvement initiative could effect a significant change in the telemetry ordering practices of the St. Vincent Hospital System.

2 Methods

A plan was devised to educate and to motivate residents to use the AHA guidelines when ordering telemetry for their patients. Prior to intervention, a survey was conducted to the entire residency on improving telemetry ordering practices. The figure below summarizes the most common resident responses.

3 Results

At the beginning of each month, a slide presentation was given on the indications for telemetry. Each physician was provided with a laminated pocket card of the AHA Telemetry guidelines, and they were reminded weekly that their prescribing practices were being monitored.

As detailed below, the average number of days spent on telemetry in the experimental group was shorter by 2.07 days compared to the number of days spent on telemetry in the pre-intervention group (p = 0.0001). The median number of days spent on telemetry was 2 in the experimental group and 4 in the control group. The accompanying figure shows that the median time spent on telemetry is also less in the experimental group.

4 Conclusion

While the results of this study are very simple, their impact has remarkable implications. Reducing the time patients spend on telemetry by an average of 2 days would lead to significant cost savings annually. If our experimental intervention were implemented to all hospital patients and using the sample population from the control group, it is estimated that St. Vincent could save over $200,000 annually (see chart below). Does reducing the amount of telemetry usage lead to more patient harm? The reason the AHA published its Appropriate Use Recommendations was to prevent unnecessary interventions, which could lead to adverse events.

This study, by using the AHA Guidelines to steer telemetry ordering and use, aims to minimize patient harm while at the same time reducing frivolous spending by St. Vincent Hospital.

5 Sources

Recurrent syncope and ventricular dysrhythmia in young adults: complications from chronic loperamide abuse

Issa Kutkut1, James Mowry2, Daniel E. Rusyniak2

1Department of Internal Medicine, Indiana University School of Medicine, Indianapolis, Indiana; 2Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis, Indiana

Introduction

Loperamide is an inexpensive OTC anti-diarrheal agent
- Inhibits intestinal peristalsis by binding µ-opioid receptors
- Massive doses overcome its poor intestinal absorption
- Promoted on Internet forums as a way to get high or avoid opioid withdrawal symptoms
- Chronic abuse can cause prolonged QTc, ventricular dysrhythmias, and subsequent death

Methods

• Literature review for relevant studies performed by searching Ovid MEDLINE and PubMed databases (1946 to September Week 2 2016)
• Data represented in graphs was obtained from National Poison Data System, Indiana Poison Center

Data

• Loperamide abuse cases have increased nationally: 16 cases in 2010 vs. 93 in 2016
• Similar trend in Indiana:
  - Adults (ages 23 – 40)
  - Majority had serious medical complications (6/8 cases)
  - 3/8 cases had recurrent syncope and prolonged QTc:
    - 200mg daily – QTc= 702ms
    - 300mg daily – QTc= 704ms
    - 200mg daily – QTc= 606ms → death (case discussed here)

Case

Presentation
• 34 year-old male, found unresponsive at home by his mother
• Medics found him in ventricular fibrillation cardiac arrest
• Return of systemic circulation after intubation and ACLS

Past Medical History
• Opioid addiction
• Loperamide abuse (200mg/day) for the past few years to help prevent opioid withdrawal
• Two previous episodes of syncope with seizure-like activity and 2 previous emergency department evaluations

Hospital Course
• ICU care, intubated, sedated
• Prolonged QTc (606ms), frequent runs of non-sustained ventricular tachycardia, and recurrent myoclonic jerks

Treatment
• Hypothermia protocol
• Isoproterenol infusion to prevent further episodes of ventricular tachycardia → normalization of QT interval
• Electrolytes monitored closely and repleted accordingly

Outcome
• Signs of dysautonomia without signs of neurological recovery or purposeful movement
• Brain imaging: anoxic injury
• Care withdrawn on day 21 of hospitalization

Conclusion

Healthcare providers should be aware of the increasing problem of loperamide abuse and its under-recognized cardiac toxicity. This should be considered a potential cause of prolonged QTc especially among patients with a history of opioid dependence and recurrent syncope.

References

A Rare Case of Cushing’s Syndrome: Not Just a Pulmonary Nodule

Andrew Wiele, DO
Indiana University School of Medicine and Indiana University Health, Indianapolis, Indiana

INTRODUCTION

Cushing’s syndrome is a rare clinical entity characterized by cortisol excess that leads to a distinct set of signs and symptoms. While pituitary adenomas account for most cases of endogenous adrenocorticotropic hormone (ACTH) dependent Cushing’s syndrome, various tumors can also secrete ACTH. This case highlights a classic presentation of Cushing’s syndrome from an unlikely source in a college-aged male.

CASE

A 21 year old male with a history of nephrolithiasis and a solitary pulmonary nodule presented to the hospital with a myriad of complaints, including chronic fatigue, progressive fifty pound weight gain, and weakness for nearly two years. He attributed these symptoms to the stress of college, but weeks before arrival began experiencing intermittent headaches, blurry vision, chest pain, abdominal cramping, and dyspnea on exertion. He also noted worsening facial acne, stretch marks on his abdomen, and skin discoloration to his legs. Physical exam revealed a tachycardic (110 beats/min) and hypertensive (198/136 mmHg) male in no acute distress, a round and erythematous face, gynecomastia, abdominal striae, central obesity, and thin extremities.

On admission he was hypokalemic (potassium: 2.8 mEq/L) and hyperglycemic (serum glucose: 122 mg/dL). Low and high dose dexamethasone suppression tests failed to decrease serum cortisol (cortisol: 25 mcg/dL and 18.4 mcg/dL, respectively); 24 hour urine free cortisol (874 mcg/24hr) and ACTH (157 mcg/dL) were also significantly elevated. A fine needle aspirate of the 1 cm left lower lobe nodule was obtained after imaging was negative for other masses. Pathology revealed a well-differentiated neuroendocrine tumor that stained positive for ACTH. Video assisted thoracoscopic lobectomy confirmed the diagnosis and revealed lymph node metastasis.

His post-operative course was complicated by thoracic vertebral compression fractures from osteoporosis and functional adrenal insufficiency, but he was quickly weaned off medications for glucose and blood pressure control. At three month follow up he was off steroids, his back was healing, and he was re-enrolled in school. Endocrinology and oncology continue to monitor his recovery.

Figure 1: Physical exam findings of classic Cushingoid features.

Figure 2: Fine needle aspirate of left lower pulmonary nodule. A: H&E showcasing nested cells. B: Chromogranin and C: Synaptophysin staining demonstrating neuroendocrine origin. D: Patchy positivity for ACTH staining.

Figure 3: Clinical decision-making chart for the differential diagnosis of confirmed Cushing’s syndrome.

DISCUSSION

Paraneoplastic Cushing’s syndrome caused by an ACTH secreting bronchopulmonary carcinoid tumor is a rare clinical occurrence, especially in young people.1,2 The worldwide incidence of these tumors is 0.2-2/100,000 individuals annually and encompasses approximately 2% of all primary lung cancers.2,3 Only 5% of bronchopulmonary carcinoid tumors are associated with ACTH production, leaving this subset of patients to comprise under 1% of all those with Cushing’s syndrome.4,5 Furthermore, multiple case series report nearly half of all patients diagnosed with a bronchopulmonary carcinoid tumor present with obstructive symptoms at an average age over forty.6,7 While this case is an extremely rare presentation of an already uncommon disease, it more importantly stresses that even a small pulmonary nodule should not be overlooked in those with Cushingoid features.

Figure 4: Chest CT. DOTACTescan was also positive for left lower pulmonary nodule.

REFERENCES