MECHANISMS OF HUMAN DISEASE AND PHARMACOLOGY & THERAPEUTICS

CASE-BASED SMALL GROUP DISCUSSION

SESSION XIII
MHD II

April 24, 2015

STUDENT COPY
**Case 1**

**HPI**
A 63-year-old man was admitted to the hospital because of paresthesias, difficulty drinking liquids, and anxiety.
Two weeks before presentation the patient developed a transient pruritic rash on his left shoulder which resolved without intervention. He had no associated fever, chills, vomiting, diarrhea, pharyngitis, or focal motor deficits.
The patient subsequently felt well until 4 days before admission, when aching developed in his left elbow, which improved with ibuprofen. The next day, right-elbow discomfort reoccurred, and he had decreased appetite. Two days before admission, he noted difficulty forming words, mild light-headedness, intermittent tremulousness and mild recurrent pain in both elbows. An attempt to drink a glass of water precipitated a gagging sensation. He had difficulty breathing and could not swallow the water. The choking sensation resolved when he spat out the water, but it recurred with subsequent attempts. He stopped drinking liquids and became increasingly anxious. One day before admission, he was unable to shower because of increased anxiety and noted intermittent decreased fluency in his speech and pruritus at the nape of his neck.
He had not traveled internationally in the past decade.
He had no history of animal bites; however, bats had been seen in his home and in a barn where he had worked several times during the previous year.
He was concerned that he was having a stroke, and he drove to the emergency department.

**PMHx**
Hypertension
Chronic ptosis of the right eyelid
Tick bite 6 months prior for which doxycycline had been administered.

**Medications**
Hydrochlorothiazide
low-dose aspirin daily

**Vaccinations**
He had received influenza and tetanus vaccinations within the past year.

**Allergies**
He has no known drug allergies.

**Social history**
He drinks alcohol occasionally,
He stopped smoking 25 years earlier
He does not use illicit drugs.
He lives with his wife in an old house in a semirural region of New England

**Family hx** – father had a history of lung cancer
Physical Examination
Temperature 37.8°C, the blood pressure 111/81 mm Hg, pulse 97 beats per minute, respiratory rate 18 breaths per minute, oxygen saturation 96% while the patient was breathing room air.

He was intermittently very anxious and hyperventilating. When given a cup of water or juice, he gagged as the cup neared his mouth and coughed while attempting to drink, with improvement after he expectorated the liquid. He was able to swallow solids. Other findings included ptosis of the right eyelid, mild facial twitching, postural hand tremors, and dysmetria on finger–nose–finger and heel-to-shin testing, without truncal ataxia. Deep tendon reflexes were symmetrically hyperactive throughout; plantar reflexes were flexor.

There was mild difficulty with tandem walking. The patient’s speech was rushed and fluent, except for occasional slurred words and pauses for word finding. The remainder of the general and neurologic examination was normal.

Laboratory Evaluation
WBC  12,000 mmol/l
Differential
Neutrophils  75.3%
Lymphocytes  17.4%
Monocytes  6.5%
Eosiophils  0.6%
Basophil  0.2%

Hgb, hct, plt count normal

Na  141 mmol/l
K  3.4 mmol/l
Cl  100 mmol/l
Co2  28 mmol/l
Glucose  121 mmol/l

Total protein, albumin, creatine kinase, troponin T, tests of coagulation, renal function, and liver function were normal.

A chest radiograph was normal. Computed tomography of the head without the administration of contrast was normal.

Hospital day 1 – Patient was conversant and had increasing anxiety and discomfort from ambient noises including hospital monitor alarms. Evaluation by a speech pathologist revealed severe anxiety related to swallowing liquids (characterized by physically aversive behaviors when liquids began to approach his facial area) without evidence of focal dysphagia, dysarthria, or an anatomical contraindication to swallowing.
Hospital Day 2 - Early in the morning the temperature rose to 38.2°C. The patient was tremulous, agitated, oriented but confused, and unable to give a clear history. After premedication with lorazepam and haloperidol, a lumbar puncture was performed. The opening pressure was 33 cm of water.

**CSF**

- Color: Colorless
- Xanthochromia: None
- RBC count: 2
- WBC count: 27
  - Lymphocytes 69%
  - Monocytes: 31%
- Protein: 51mg/dl
- Glucose: 84mg/dl
- Varicella zoster virus by PCR: Negative
- HSV by PCR: Negative

Cytologic examination and flow cytometry of the CSF showed no abnormalities.

Shortly after the lumbar puncture, the patient became cyanotic. The systolic blood pressure was 240mmHg, pulse 160 (supraventricular tachycardia on EKG), respiratory rate 40, oxygen saturating 40% on RA. The pulse suddenly decreased to 60 then returned to 150. A repeat CXR showed perihilar fullness and loss of definition of the pulmonary vasculature consistent with pulmonary edema.

**Educational Objectives**

1. Summarize the key features of this case.

2. The physicians caring for the patient had several considerations in the formulation of the differential diagnosis which included bacterial toxins, alcohol-related, drug reactions and viral infectious causes of encephalitis.

   a. Which bacterial toxin mediated infections would have as manifestations dysfunction of the nervous system? Are any of them consistent with this patient’s presentation?
b. How could alcohol use be related to this patient’s presentation?

c. Are there any drug reactions to consider that may manifest with symptoms/signs similar to this patient’s presentation?

d. What cause(s) of viral encephalitis you would put highest on the differential? Why?

3. Discuss the pathogenesis of infection with the most likely etiologic virus, including the incubation period.

4. A biopsy of the patient’s neck skin was performed. What test(s) would you recommend be done on the biopsy to confirm the most likely diagnosis? Are there other tests that could be performed to support the diagnosis antemortem?
5. If this patient had presented immediately after known exposure to the virus, what treatment should he have received? What treatment is available after symptoms develop?

6. Should the patient have been in isolation during the hospitalization?

7. Is there a way to prevent infection with this agent? Who should routinely receive vaccine against this virus? What type of vaccine is it?

8. The patient died and consent for autopsy was obtained from the patient’s wife. What are the key findings in the brain you would expect?

9. Unknown - Students will be provided question during small group session. It relates to viral vaccines.

Case 2
History of Present Illness
A 52-year old man presents to a primary care physician to establish care. He has not seen a
physician for >20 years and thinks he should “check-in” with one. He has been feeling in his usual state of health and has no specific complaints.

**PMHx**
No known chronic medical problems, no prior surgeries

**Medications**
Acetaminophen Extra-strength tablet as needed for “aches and pains” – rarely takes Multivitamin “when I remember”

**Allergies**
Penicillin – developed a rash as a child

**Social History**
Tobacco use – never
Alcohol use – few beers less than 1 time per week
Illicit drug use – denies ever using
Born in the Azures and immigrated to the US at 19 years of age
Married
Has 1 son and 1 daughter
Works as a custodian in a middle school

**Family history**
Father died of lung cancer at 68 years of age
Mother had undergone CABG, is in her 70s
Brother – has hypertension and kidney disease
2 sisters – alive and well
Children – healthy

**Review of Systems**
General – stable weight, no weakness, no fevers or chills or nightsweats
Skin – no new rashes, lumps, dryness. Has had red spots on his stomach and groin area for years
HEENT - no changes in vision, no dizziness, lightheadedness, kids tell him he is getting hard of hearing, he does not think so
Head - no Headaches, no head injury
Respiratory – no problems with cough, SOB
Cardiovascular – no chest pain or discomfort, no dyspnea, orthopnea, paroxysmal nocturnal dyspnea, edema; sometimes thinks he has palpitations for a brief time but they go away before he does anything about them
Gastrointestinal- normal bowel movements, no change in color and size of stools, no abdominal pain, nausea or vomiting
Urinary -no pain on urination, no hematuria, gets up once at night to urinate, good stream
Genital- no pain or masses, no hernias, no problems with erection
Musculoskeletal – occasional backache, knee aches if works especially hard, no swelling or redness of joints
Neurologic – no loss of sensation, tingling or "pins and needles," tremors or other involuntary movements.
Hematologic – no easy bruising or bleeding
Endocrine. – no excessive thirst or hunger, always feels hot – has been going on for years
Psychiatric – no Nervousness, tension; no mood or memory problems

Physical exam
Patient appears well
BP 112/70; pulse 62, respirations 18, afebrile
Height 5’11” Weight 200 pounds

Head and neck – Thyroid gland normal; no lymphadenopathy
Lungs – clear to auscultation and percussion
Cardiovascular:
Heart –Normal S1 and S2, audible fourth heart sound, no murmurs, apical impulse diffuse and laterally displaced
No jugular venous distention
Normal peripheral pulses
Abdomen – normal
Skin – lower abdomen and inguinal region with multiple 2- to 7-mm, red to purple, hyperkeratotic and coalescing papules

Learning Objectives

1. To what do you attribute the findings on heart exam? How could you support/confirm your clinical impression? What is the differential diagnosis?
Diagnostic tests are ordered by the physician. The patient returns for follow-up 2 weeks later. He has no new concerns. His blood pressure in the right arm is 114/70; left arm 116/72. Physical exam is unchanged. Funduscopic exam is normal.

The physician reviews the following with the patient:

**EKG – at end of case**

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>100 mg/dl</td>
</tr>
<tr>
<td>Blood Urea Nitrogen</td>
<td>12 mg/dl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.8 mg/dl</td>
</tr>
<tr>
<td>Calcium</td>
<td>9.3 mg/dl</td>
</tr>
<tr>
<td>Sodium</td>
<td>134 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.9 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>106 mmol/L</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td>21 mmol/L</td>
</tr>
</tbody>
</table>

**CBC**

- WBC: 6.1 [4.0-10.0] k/ul
- RBC: 3.80 [3.60-5.50] m/ul
- Hgb: 12.8 [12.0-16.0] gm/dl
- Hct: 37.9 [34.0-51.0] %
- MCV: 91 [85-95] fl
- MCH: 29.1 [28.0-32.0] pg
- MCHC: 33.7 [32.0-36.0] gm/dl
- RDW: 31 [11.0-15.0] %
- Plt Count: 161 [150-400] k/ul

**Basic Metabolic Panel**

- Glucose: 100 [70-100] mg/dl
- Blood Urea Nitrogen: 12 [7-22] mg/dl
- Creatinine: 1.8 [0.7-1.4] mg/dl
- Calcium: 9.3 [8.5-10.5] mg/dl
- Sodium: 134 [136-146] mmol/L
- Potassium: 3.9 [3.5-5.3] mmol/L
- Chloride: 106 [98-108] mmol/L
- Carbon Dioxide: 21 [20-32] mmol/L

**LIVER FUNCTION PANEL**

- Albumin: 3.8 [3.6-5.0] gm/dl
- Bilirubin, Total: 1.2 [0.2-1.4] mg/dl
- Bilirubin, Direct: 0.2 [0.0-0.3] mg/dl
- Alkaline Phosphatase: 98 [30-110] iu/l
- AST (SGOT): 26 [5-40] iu/l
- ALT (SGPT): 29 [7-35] iu/l
- Protein, Total: 6.8 [6.5-8.3] gm/dl

**UA w/Micro**
A transthoracic echocardiogram showed severe concentric biventricular hypertrophy with normal systolic function, moderate to severe biatrial enlargement. No valvular abnormalities.

2. Based on the data provided, develop a problem list.

3. Return to your differential diagnosis of the main cardiac problem. What have you now potentially “ruled out”? Why was a funduscopic exam performed?

The physician discusses the “next steps” with the patient who returns 2 weeks later. This time his brother accompanies him and tells you that he recently had a “kidney biopsy”. He
has a copy of the biopsy report which he shows you. You note on electron microscopy findings the presence of podocyte and distal tubule intra-cytoplasmic, intralysosomal inclusions, composed of concentric layers with an onion skin appearance.

4. Is this information helpful? What disease processes are you considering? Why? Which do you favor based on the available data?

5. What treatment do you recommend for the underlying disease process?

EKG

Case 3
A 35 year-old woman presented to the Emergency Department in January with fever and a left focal seizure. She had been previously healthy, but developed fever, headache and malaise one
day before the seizure episode. She takes no medications regularly. She has not recently traveled. She is married. There is no history of illicit drug use.

In the Emergency Department, she was disoriented and lethargic with a temperature of 39°C. Skin, heart, lung, and abdominal examinations were normal. The patient did not cooperate with funduscopic exam or neurologic exam. She was moving all 4 of her extremities.

**Students will be provided remainder of data and questions during the small group session.**

“**Case 4**”– **Beyond multiple choice**

Students are asked to each develop 2 questions before the small group session which they will direct to the student sitting to the left or right of them (facilitator choice for the session).

Questions are to be related to small group material (ie the organ system) from year 1 (anatomy, physiology, cell/molecular biology, immunology). So that questions have “relevance”, students are asked to derive the idea for their question from First Aid for USMLE Step 1, but further research/verify the question & answer via a text from their MS-1 year or another published text available through the LUHS library. Students should cite the resource(s) that they use and pages (when able from the online text).

After the student answers the question, they should provide a **brief** explanation for the answer.

The student who answered the question will then ask their question to the next student.

Proceed to the 2nd round with the 2nd question developed by the students.

Please be willing to post your questions/answers/references on Sakai for the class to share/review, particularly for USMLE preparation.