Neutropenic Fever

Shannon Toohey, MD, MAEd*

*University of California, Irvine, Department of Emergency Medicine, Orange, CA

Correspondence should be addressed to Shannon Toohey, MD, MAEd at stoohey@uci.edu

Submitted: July 30, 2016; Accepted: August 22, 2016; Electronically Published: September 13, 2016; https://doi.org/10.21980/J8KW2K

ABSTRACT:

Audience: This oral boards case is appropriate for all emergency medicine learners (residents and interns).

Introduction: Neutropenia is a common oncologic emergency, and it frequently develops as a result of myelosuppression from chemotherapy. Neutropenia is defined as absolute neutrophil count (ANC) <1000/mm^3, with severe neutropenia being defined as ANC<500/mm^3. Patients with fever and neutropenia should be presumed to have infectious etiology and started on antibiotics immediately. The 48-hour mortality associated with an untreated infection is 20%-50%.

Objectives: At the end of this oral boards session, the learner will: 1) appropriately assess a potentially ill patient in oral boards format; 2) order appropriate imaging and labs for a patient with suspected neutropenic fever; 3) consent patient for lumbar puncture and describe how to perform the procedure; 4) execute management and disposition of a patient with neutropenic fever.

Method: Oral boards case

Topics: Neutropenic fever, chemotherapy, oncology, infectious disease, sepsis.

USER GUIDE

List of Resources:

Learner Audience:
Interns, Junior Residents, Senior Residents

Time Required for Implementation:
Case: 15 minutes
Debriefing: 5 minutes
Learners per instructor: This is best used to practice oral boards with 1 learner, but could be used in a small group setting with as many as 3 learners.

Topics:
Neutropenic fever, chemotherapy, oncology, infectious disease, sepsis.

Objectives:

1. Learners will learn to appropriately assess a potentially ill patient in an oral boards format.
2. Learners will order appropriately imaging and labs for a patient with suspected neutropenic fever.
3. Learners will appropriately consent patient for lumbar puncture and describe how to perform the procedure.
4. Learners will execute management and disposition a patient with neutropenic fever.

Linked objectives and methods:
This oral board case allows learners to have a simulated first-hand experience managing a patient with neutropenic fever. Completion of the oral board case allows learners to evaluate a patient with neutropenia and symptoms concerning for meningitis. During the case they will assess the patient (objective 1), recognize possible neutropenic fever and order appropriate imaging and labs (objective 2). When no source is found they should consent the patient for a lumbar puncture (LP) and describe the procedure (objective 3). Lastly, they will need to appropriate treat and disposition the patient (objective 4).

Debriefing the case will allow the instructor to clarify any confusion or gaps in knowledge on the diagnosis and management of patients with neutropenic fever and the evaluation and differential diagnosis for patients with altered mental status.

Recommended pre-reading for instructor:
Any resource reviewing neutropenic fever would be appropriate, please see some suggestions below:

1. Lin M. Paucis verbis: neutropenic fever in cancer patients. Academic Life in Emergency Medicine. https://www.aliem.com/2011/paucis-verbis-neutropenic-fever-in-cancer-patients/. Published October 7, 2011. Accessed August 12, 2016.
2. Sperling JD. Introduction to oncologic emergencies. In: Adams JG, Barton ED, Collings JL, DeBlieux PM, Gisondi MA, Nadel ES, eds. *Emergency Medicine: Clinical Essentials.* 2nd ed. Philadelphia, PA: Elsevier; 2013:1666-1668.
3. Lewis GM, Chai A. Introduction to oncologic emergencies. In: Wolfson AB, ed. *Harwood-Nuss' Clinical Practice of Emergency Medicine*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:987.
4. Ugras-Rey, SS. Selected oncologic emergencies. In: Walls RM, Hockberger RS, Gausche-Hill M, et al. eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier; 2014:987.

Results and tips for successful implementation:
This case was initially presented as an oral board case in a small group setting with 19 learners. It was positively received by residents who found it a useful review and practice for oral boards.

The case was straight-forward for senior residents, but slightly more difficult for novice learners. One issue was novice learners forgot to check platelet count before performing the LP, however, this is a good learning point for them. While this case is best done as an oral boards case, it can also be done as a simulation case or small group session. It is important to debrief the case with the learner after completion of the case or provide post-case reading material.

Pearls:

- Chemotherapy causes neutropenia in 10%-15% of patients with solid tumors and greater than 80% of those with hematologic malignancies.
- The definition of neutropenic fever is a single temperature greater than 38.3°C or a sustained fever greater than 38°C (100.4°F) for more than 1 hour, with an absolute neutrophil count less than 500 cells/mm^3, or less than 1000 cells/mm^3 with a predicted nadir of less than 500 cells/mm^3.
- Neutropenic patients should be placed in single rooms with positive air pressure.
- The mortality rate of patients with neutropenic fever who are untreated is 20%-50%.

- Work-up for the fever includes complete blood count (CBC), blood urea nitrogen (BUN)/Creatinine (Cr), electrolytes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, urinalysis, chest X-ray, two blood cultures (one from central line if present).
    - Consider LP if concern for central nervous system infection.
        - Remember to check platelet counts and coagulation studies before performing an LP.
- Antibiotic therapy should include an anti-pseudomonal beta-lactam such as cefepime or a carbapenem.
    - Consider adding gentamicin for high-risk patients.
    - Consider adding vancomycin if hospital-associated pneumonia, soft tissue infection or for patients with an indwelling catheter or history of MRSA.
- If the patient has a central line-associated blood stream infection, the catheter does not necessarily need to be removed.
- If patient is septic, treat as you would any other septic patient, with early aggressive fluid resuscitation, goal-directed therapy, and vasopressors, if needed for hypotension.
- Afebrile patients with neutropenia and suspicion of infection should also be cultured and treated with broad-spectrum antibiotics.
- Most patients with neutropenic fever require admission.
- Several trials have recently introduced a prediction tool to assess patients suitable for outpatient therapy; however, this plan would be made with a patient's oncologist. Contraindications for outpatient therapy include: history of noncompliance, inability to care for oneself, lack of caregivers, lack of telephone or reliable transport, or high risk of severe infection.
    - Recommended outpatient antibiotics are a combination of ciprofloxacin and amoxicillin/clavulanic acid.

References/suggestions for further reading:

1. Lin M. Paucis verbis: neutropenic fever in cancer patients. Academic Life in Emergency Medicine. https://www.aliem.com/2011/paucis-verbis-neutropenic-fever-in-cancer-patients/. Published October 7, 2011. Accessed August 12, 2016.
2. Kulchycki, LK. Immunosuppression. In: *Rosen & Barken's 5-Minute Emergency Medical Consult*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:592-593.
3. Sperling JD. Introduction to oncologic emergencies. In: Adams JG, Barton ED, Collings JL, DeBlieux PM, Gisondi MA, Nadel ES, eds. *Emergency Medicine: Clinical Essentials.* 2nd ed. Philadelphia, PA: Elsevier; 2013:1666-1668.
4. Lewis GM, Chai A. Introduction to oncologic emergencies. In: Wolfson AB, ed. *Harwood-Nuss' Clinical Practice of Emergency Medicine*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:987.
5. Ugras-Rey, SS. Selected oncologic emergencies. In: Walls RM, Hockberger RS, Gausche-Hill M, et al. eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier; 2014:987.

FOR EXAMINER ONLY

Oral Case Summary

Diagnosis: Neutropenic Fever

Case Summary: A 47-year-old male with a history of pancreatic cancer on chemotherapy is brought to the emergency department for a fever of 102.4°F at home. The patient last received chemotherapy five days ago. He also notes he has a headache, photophobia, nausea and vomiting. He denies other infectious symptoms. His physical exam is unremarkable.

Order of Case: The learner should quickly evaluate the patient's general appearance as well as the ABCs. The learner should then take a history and perform a physical exam including a neurologic examination. The learner needs to recognize the possibility of neutropenic fever and order labs, chest X-ray, and urinalysis. Given the patient's headache, they should order a head computed tomography (CT) to evaluate for brain metastases or intracranial hemorrhage. Learners should check platelets and coagulation studies, and consent the patient for and perform a lumbar puncture. Other than dehydration and significant neutropenia, the work-up will be negative with no clear source of infection. The patient should be admitted for intravenous (IV) antibiotics for presumed bacteremia.

Disposition: Admission

Critical Actions:

1. Perform a complete history and physical exam, including neurologic examination.
2. Order appropriate labs and imaging: CBC, electrolytes, BUN, Cr, chest X-ray, CT head, and coagulation studies.
3. Consent patient for a lumbar puncture.
4. Describe how to perform a lumbar puncture.
5. Order appropriate IV antibiotics.
6. Admit the patient to the hospital.

FOR EXAMINER ONLY

Historical Information

Chief Complaint: Fever

History of present illness: A 47-year-old male presents to the emergency department with fever up to 102.4°F at home. He has pancreatic cancer and is receiving chemotherapy, most recently five days ago. The patient reports feeling generally tired and weak today, then took his temperature and found it to be 102.4°F. He also reports a sharp, diffuse headache, associated with photophobia, nausea and several episodes of non-bilious, non-bloody emesis. He denies cough, congestion or chest pain, but does endorse some mild shortness of breath in the past few hours. He denies abdominal pain, diarrhea, dysuria, frequency or urgency.

Past Medical history: Metastatic pancreatic cancer, status post pancreaticoduodenectomy (Whipple), now on chemotherapy, hypertension, diabetes type 1
Past Surgical history: Pancreaticoduodenectomy (Whipple), appendectomy
Patients Medications: Ondansetron, morphine, reglan, lisinopril, insulin
Allergies: No known drug allergies
Social history:

- Smoking: denies
- Tobacco: denies
- Drug use: denies

Family history: Reviewed and non-contributory

FOR EXAMINER ONLY

Physical Exam Information

Vitals: Heart rate (HR) 119 Blood pressure (BP) 101/54 Respiratory rate (RR) 26
Temperature (T) 39.1°C Oxygen saturation (O_2Sat) 98%
Weight: 69kg
General appearance: awake, alert, cooperative, in mild distress
Primary survey:

- **Airway:** patent, protected and phonating.
- **Breathing:** mild tachypnea, breath sounds bilaterally without wheezing or rhonchi.
- **Circulation:** tachycardic, bounding femoral pulses.

Physical examination:

- **General appearance:** awake, alert, cooperative, in mild distress.
- **Head ears, eyes, nose and throat (HEENT)**:
  - **Head:** normocephalic, atraumatic.
  - **Eyes:** pupils are equally round and reactive to light with mild photophobia.
  - **Ears:** within normal limits.
  - **Nose:** within normal limits.
  - **Oropharynx/Throat:** dry mucous membranes, no erythema or exudates of throat
- **Neck:** no pain with flexion or extension.
- **Chest:** mild tachypnea, breath sounds bilaterally without wheezing, rales or rhonchi; port-a-cath in place in right chest wall without surrounding erythema or drainage.
- **Cardiovascular:** tachycardic, regular rhythm, no murmurs.
- **Abdominal:** within normal limits.
- **Genitourinary:** within normal limits.
- **Rectal:** within normal limits.
- **Extremities:** within normal limits.
- **Back:** within normal limits.
- **Neuro:** alert and oriented x 3, cranial nerves 2-12 intact, 5/5 strength all four extremities, sensation intact.
- **Skin:** mild diaphoresis.
- **Lymph:** within normal limits.
- **Psych:** within normal limits.

FOR EXAMINER ONLY

Critical Actions and Cueing Guidelines

1. **Perform a complete history and physical exam, including neurologic examination.**
   The learner should perform a thorough history and physical exam, including a neurologic examination given the patient's complaint of fever.
   a. Cueing Guideline:
      If the learner has not yet completed a history and physical, the examiner may cue them by having the wife ask "doctor, what do you think is causing the fever?"

2. **Order appropriate labs and imaging: CBC, electrolytes, BUN, Cr, chest x-ray, CT head, and coagulation studies.**
   The learner should order appropriate labs and imaging to work up a patient with neutropenic fever and headache.
   a. Cueing Guideline:
      If the learner has not yet addressed this issue, the examiner may cue them by having the nurse ask "do you want to place any orders, doctor?"

3. **Consent patient for a lumbar puncture.**
   The learner should recognize that a lumbar puncture is necessary and consent the patient appropriately. Score down if the learner does not appropriately consent.
   a. Cueing Guideline:
      If the learner has not yet decided to perform a lumbar puncture, the examiner may cue them by having the patient ask "why would I have a fever and a headache?"

      If the learner is about to perform the lumbar puncture but has not appropriately consented the patient, the examiner may cue them by having the wife ask "what are the risks of the procedure?"

4. **Describe how to perform a lumbar puncture.**
   The learner should explain the steps of completing a lumbar puncture.
   a. Cueing Guideline:
      If the learner does not describe how to perform a lumbar puncture in detail, the examiner should say: "describe the procedure."

FOR EXAMINER ONLY

5. **Order appropriate IV antibiotics.**
   The learner should order appropriate IV antibiotics, such as cefepime or a carbapenem. Score down if the learner does not order antibiotics or orders antibiotics that do not have appropriate coverage.
   a. Cueing Guideline:
      If the learner has not ordered IV antibiotics, the examiner may cue them by asking "is there anything else you would like to order?"

6. **Admit to the hospital.**
   The learner should recognize the patient has neutropenic fever with moderate to severe symptoms and hypotension, and requires admission.
   a. Cueing Guideline (if applicable):
      If the learner has not yet admitted the patient, the examiner may cue them by having the nurse ask "what is the disposition for the patient?"

ORAL BOARDS ASSESSMENT

Neutropenic Fever

Learner: _____

Critical Actions:

- ☐ Perform a complete history and physical exam, including neurologic examination.
- ☐ Perform an accucheck (point of care blood glucose)
- ☐ Order appropriate labs and imaging: CBC, electrolytes, BUN, Cr, chest x-ray, CT head, and coagulation studies.
- ☐ Consent patient for a lumbar puncture.
- ☐ Describe how to perform a lumbar puncture.
- ☐ Order appropriate IV antibiotics.
- ☐ Admit the patient to the hospital.

Summative and formative comments:

Milestone assessment:

	Milestone	Did not achieve level 1	Level 1	Level 2	Level 3
1	**Emergency Stabilization (PC1)**	☐ Did not achieve Level 1	☐ Recognizes abnormal vital signs	☐ Recognizes an unstable patient, requiring intervention Performs primary assessment Discerns data to formulate a diagnostic impression/plan	☐ Manages and prioritizes critical actions in a critically ill patient Reassesses after implementing a stabilizing intervention
2	**Performance of focused history and physical (PC2)**	☐ Did not achieve Level 1	☐ Performs a reliable, comprehensive history and physical exam	☐ Performs and communicates a focused history and physical exam based on chief complaint and urgent issues	☐ Prioritizes essential components of history and physical exam given dynamic circumstances

Standardized assessment form for oral boards cases. JETem © Developed by: Megan Osborn, MD, MHPE; Shannon Toohey, MD; Alisa Wray, MD
Toohey S. Neutropenic Fever. JETem 2016. 1(2):O1-20. https://doi.org/10.21980/J8KW2K

ORAL BOARDS ASSESSMENT

Neutropenic Fever

Learner: _____

	Milestone	Did not achieve level 1	Level 1	Level 2	Level 3
3	**Diagnostic studies (PC3)**	☐ Did not achieve Level 1	☐ Determines the necessity of diagnostic studies	☐ Orders appropriate diagnostic studies Performs appropriate bedside diagnostic studies/procedures	☐ Prioritizes essential testing Interprets results of diagnostic studies Considers risks, benefits, contraindications, and alternatives to a diagnostic study or procedure
4	**Diagnosis (PC4)**	☐ Did not achieve Level 1	☐ Considers a list of potential diagnoses	☐ Considers an appropriate list of potential diagnosis May or may not make correct diagnosis	☐ Makes the appropriate diagnosis Considers other potential diagnoses, avoiding premature closure
5	**Pharmacotherapy (PC5)**	☐ Did not achieve Level 1	☐ Asks patient for drug allergies	☐ Selects an appropriate medication for therapeutic intervention, considering potential adverse effects	☐ Selects the most appropriate medication(s) and understands mechanism of action, effect, and potential side effects Considers and recognizes drug-drug interactions
6	**Observation and reassessment (PC6)**	☐ Did not achieve Level 1	☐ Reevaluates patient at least one time during the case	☐ Reevaluates patient after most therapeutic interventions	☐ Consistently evaluates the effectiveness of therapies at appropriate intervals
7	**Disposition (PC7)**	☐ Did not achieve Level 1	☐ Appropriately selects whether to admit or discharge the patient	☐ Appropriately selects whether to admit or discharge Involves the expertise of some of the appropriate specialists	☐ Educates the patient appropriately about their disposition Assigns patient to an appropriate level of care (ICU/Tele/Floor) Involves expertise of all appropriate specialists

Standardized assessment form for oral boards cases. JETem © Developed by: Megan Osborn, MD, MHPE; Shannon Toohey, MD; Alisa Wray, MD
Toohey S. Neutropenic Fever. JETem 2016. 1(2):O1-20. https://doi.org/10.21980/J8KW2K

ORAL BOARDS ASSESSMENT

Neutropenic Fever

Learner: _____

	Milestone	Did not achieve level 1	Level 1	Level 2	Level 3
22	**Patient centered communication (ICS1)**	☐ Did not achieve level 1	☐ Establishes rapport and demonstrates empathy to patient (and family) Listens effectively	☐ Elicits patient's reason for seeking health care	☐ Manages patient expectations in a manner that minimizes potential for stress, conflict, and misunderstanding.
23	**Team management (ICS2)**	☐ Did not achieve level 1	☐ Recognizes other members of the patient care team during case (nurse, techs)	☐ Communicates pertinent information to other healthcare colleagues	☐ Communicates a clear, succinct, and appropriate handoff with specialists and other colleagues Communicates effectively with ancillary staff

Standardized assessment form for oral boards cases. JETem © Developed by: Megan Osborn, MD, MHPE; Shannon Toohey, MD; Alisa Wray, MD
Toohey S. Neutropenic Fever. JETem 2016. 1(2):O1-20. https://doi.org/10.21980/J8KW2K

Stimulus Inventory

#1 Patient Information Form

#2 Coagulation Studies

#3 Complete blood count (CBC)

#4 Basic metabolic panel (BMP)

#5 Urinalysis

#6 Chest X-ray

#7 Head CT

#8 Lumbar puncture results

Stimulus #1

Patient Information

Patient's Name: **Steve Dean**

Age: **47**

Gender: **Male**

Chief Complaint: **Fever**

Person Providing History: Patient and wife

Vital Signs:

Temp:	**39.1°C**
BP:	**101/54**
P:	**112**
RR:	**26**
Pulse Ox:	**98% on room air**
Weight:	**69kg**

Stimulus #2

Coagulation Studies

Prothrombin time (PT)	**12 second**
Partial thromboplastin time (PTT)	**29 seconds**
International normalized ratio (INR)	**0.9**

Stimulus #3

CBC

White blood count (WBC)	**1.1 x10^3/mm^3**
Hemoglobin (Hgb)	**8.9 g/dL**
Hematocrit (Hct)	**25.1%**
Platelets	**120 /mm^3**

Differential

Neutrophils	**33%**
Lymphocytes	**43%**
Monocytes	**10%**
Eosinophils	**12%**
Bands	**2%**

Stimulus #4

BMP

Sodium (Na)	**127 mEq/L**
Potassium (K)	**4.2 mEq/L**
Chloride (Cl)	**101 mEq/L**
Carbon dioxide (CO_2)	**23 mEq/L**
Blood urea nitrogen (BUN)	**35 mg/dL**
Creatinine (Cr)	**1.4 mg/dL**
Glucose	**149 mg/dL**

Stimulus #5

Urinalysis

Appearance	**Clear**
Color	**Yellow**
Glucose	**Neg**
Ketones	**Neg**
Specific gravity	**1.4**
Blood	**Neg**
pH	**6.3**
Protein	**Neg**
Nitrite	**Neg**
Leukocyte	**Neg**
White blood cells (WBC)	**0/high powered field (HPF)**
Red blood cells (RBC)	**0/HPF**
Squamous Cells	**0/HPF**
Bacteria	**None**

Stimulus #6

Chest X-ray

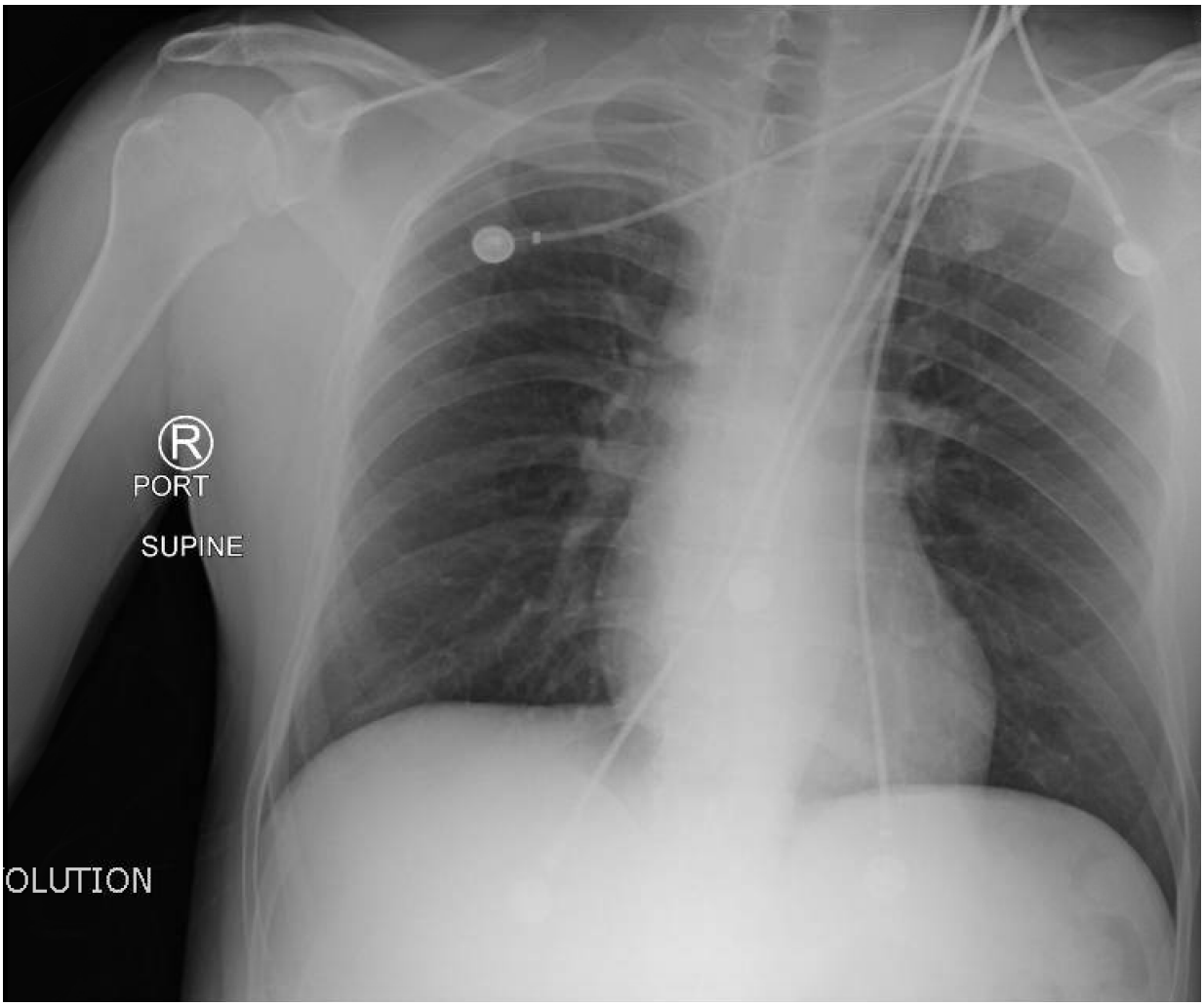
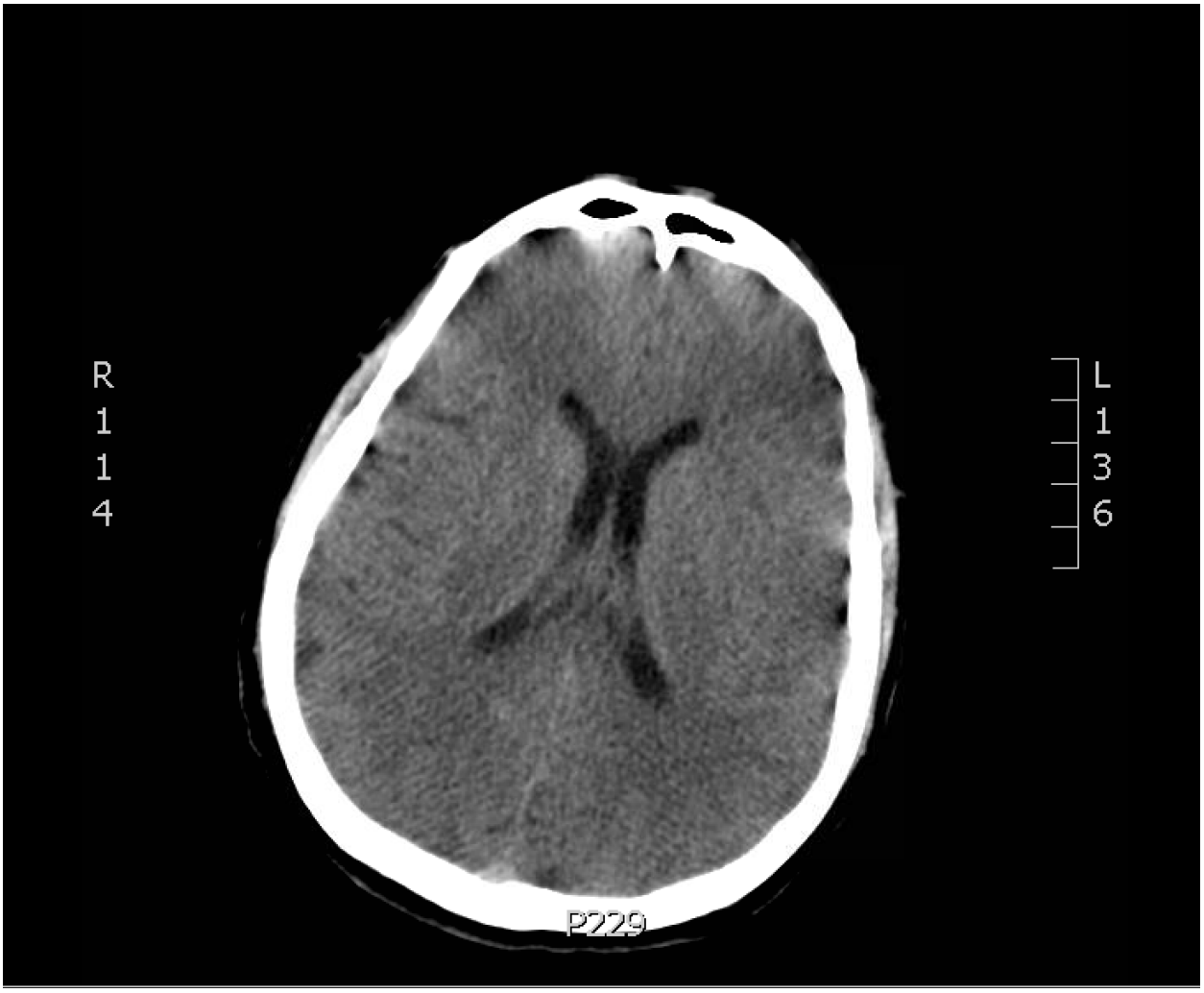


Image source: Author's own image

Stimulus # 7

Head CT



Author's own image

Stimulus # 8

Lumbar puncture results

Color	**Clear**
Opening pressure	**9 mmHg (normal 5-20)**
WBCs	**0 cells/mm^3 (normal <5)**
Glucose	**52 mg/dL (normal 40-70)**
Protein	**30 mg/dL (normal 20-50)**
Gram stain	**Negative**
Cerebral spinal fluid culture	**Pending**