Diagnostic confusion: how a common problem delayed finding the correct diagnosis

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Case presentation

- 45 year-old Hispanic man
- Brought by ambulance without acquaintances
  - Confusion and agitation
  - Found “thrashing about”
  - Incontinent of urine
- Responded to painful stimuli

Case presentation

- Past medical history
  - Hepatitis C
  - Bipolar Disorder
  - Antisocial Personality Disorder
  - Recent sinusitis
- Social History
  - Cocaine and alcohol abuse
- Recently released from inpatient treatment

Case presentation

- Medications
  - Sertraline 50 mg daily
  - Quetiapine 200 mg daily
  - Hydrocodone/acetaminophen 5/500 mg every 4 hours as needed
  - Prednisone dose pack
  - Amoxicillin/clavulanate 750/125 mg twice daily

Physical examination

- Vitals: afebrile, 124/70, P 93, R 22, 0_2 96% RA
- Gen: somnolent, responded to pain, mumbled
- HEENT: Atraumatic, pupils dilated but reactive and equal
- Neck: supple with negative Kernig and Brudzinski signs
- Neuro: localized to pain, deep tendon reflexes normal and equal

Case presentation

CBC (fishbone): WBC **13.1**, Hgb 14.8, Hct 42.4, Plt 318

Na	Cl	BUN	Glucose
145	**109**	**41**	98
4.4	**11**	**4.9**	
K	HCO_3	Cr	

Anion Gap **25**

ABG:

pH **7.27**

pCO_2 **27.6**

pO_2 **126**

HCO_3 **12.7**

UDS **negative x 3**

Tylenol neg

Salicylate neg

Ethanol neg

Lactate 0.9

Serum ketones **small**

CPK **918**

CT Head: negative for acute intracranial processes. No sinusitis.

Course

- NG lavage and activated charcoal in ED
- Admitted overnight by ED physician with diagnosis of drug use and intoxication
- Following day, the differential diagnosis was expanded to include:
  - Serotonin syndrome
  - Neuroleptic malignant syndrome
  - Drug-induced methemoglobinemia
  - Meningitis

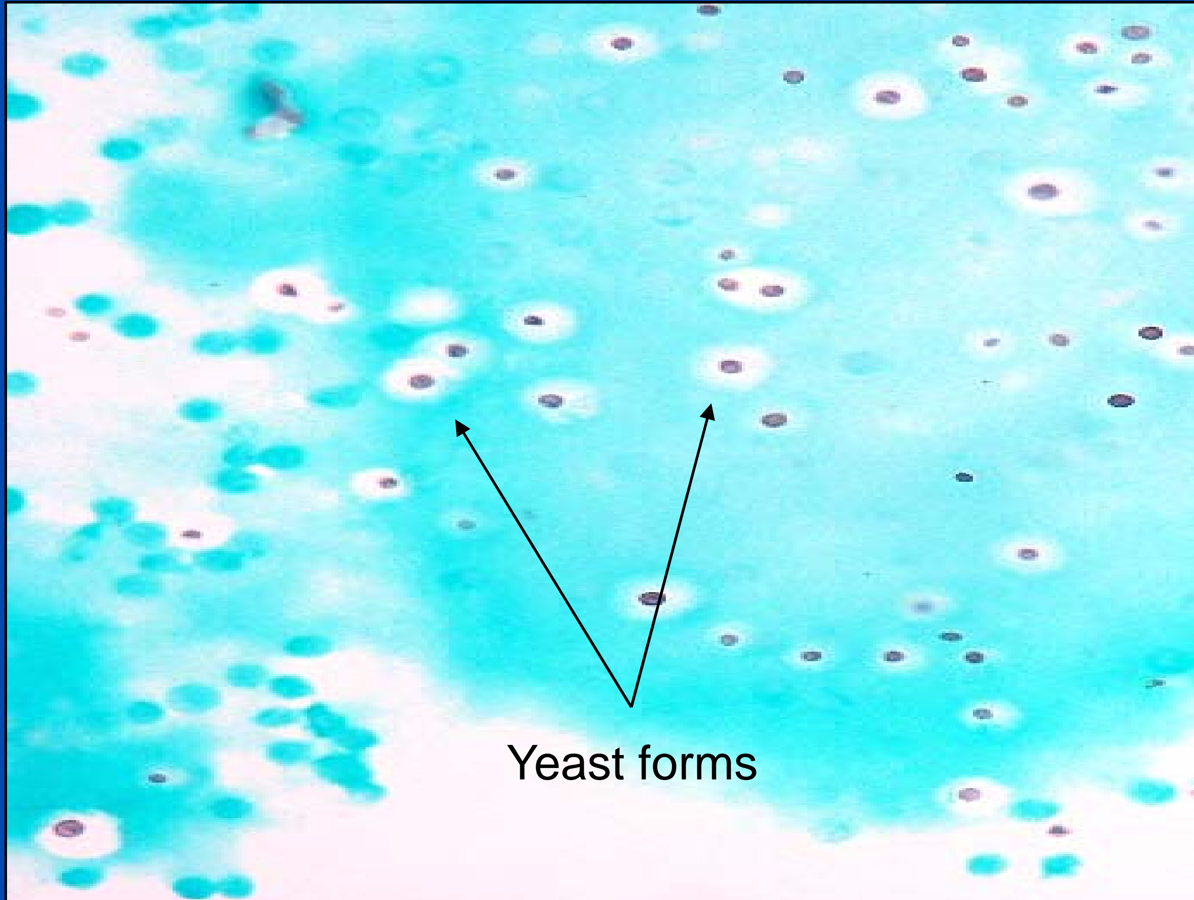
Course

- Pt's condition did not improve
- 32 hours after admission
  - Right fixed, dilated, irregular pupil
- Repeat CT head negative
- Intubated and sedated
- An LP was done that afternoon
  - Protein 370
  - Glucose 28
- Started on broad spectrum antibiotics for presumed meningitis

Course

- Other CSF results available the next morning
  - Leukocyte count 281
    - Lymphs 96%
    - Polys 4%
- Differential was broadened to include viral, fungal, and tuberculous meningitis
  - Antivirals, antifungals and 4-drug TB regimen started
  - HIV antibody and CD4 lymphocyte counts ordered

CSF cytology from this patient



Grocott's methenamine silver stain

Course

- India Ink stain of CSF positive
- CSF cryptococcal antigen titer 1:256
- HIV antibody positive
  - Quantitative HIV load 290,000
  - CD4 lymphocyte count 66

Course

- His neurological status slowly improved
- He was discharged home:
  - antiretrovirals
  - oral fluconazole
- Functioning completely independently

Cryptococcal meningitis

- Chronic headache is the most common symptom, along with fever and malaise
- Forty percent of patients have nausea and vomiting
  - A minority may have
    - Lethargy
    - Altered mentation
    - Personality changes
    - Memory loss
    - Cranial nerve palsies

Powderly, WG, et al. *Clinical Infectious Disease*. 1994, 18, 789-792.

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Recapitulation of delay in diagnosis

- Admitted overnight with working diagnosis of drug intoxication
- No improvement and new exam finding
  - CSF glucose and protein abnormal
  - Antibiotics were started
- Cell count became available the next day
  - Antiviral, antifungal and anti-TB drugs started
- HIV studies were initiated

Types of diagnostic errors

- "No fault errors"
  - Arise when the disease is silent, presents atypically or mimics a more common illness
- "System errors"
  - Occur when the diagnosis is delayed or missed because of imperfections in the health care system
- "Cognitive errors"
  - Develop from incomplete data collection or interpretation, inaccurate reasoning, or incorrect knowledge

Graber, M, et al. "Reducing Diagnostic Errors in Medicine: What's the Goal?" *Academic Medicine*. 2002, Vol 77, 981-992.

Diagnostic errors in a recent study

- Study of 100 patients who had diagnostic errors
  - Cases collected from 5 large academic tertiary care medical centers over 5 years
    - 57 quality assurance activities
    - 33 voluntary reports
    - 10 autopsy discrepancies
  - Each of these 100 patients averaged 5.9 reasons for the error in diagnosis
    - Several types of errors contributed to misdiagnosis in each patient

Graber, ML, et al. “Diagnostic Error in Internal Medicine.” *Archives of Internal Medicine.* 2005, Vol 165, 1493-1499

Common diagnostic errors that contributed to confusion in this case

- *No fault errors*
  - Masked, meaning a common diagnostic possibility hides a rare diagnosis
  - Unusual presentation
- *Cognitive factors*
  - Data gathering incomplete in history, exam or labs
  - Faulty synthesis, making the wrong diagnosis from the data
    - Failure to act sooner with delay in certain tests
- *System related errors*
  - Technical problems

Graber, ML, et al. "Diagnostic Error in Internal Medicine." *Archives of Internal Medicine.* 2005, Vol 165, 1493-1499

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Why was there diagnostic confusion in this case?

- No fault error
  - Atypical presentation
    - Headaches attributed to sinusitis
    - Lack of fever, no nuchal rigidity
  - HIV status was not known despite being a patient at the facility
- Cognitive error
  - Focus was on drug use history
  - “Tunnel vision" towards drug intoxication
  - Delay in lumbar puncture
- Systems error
  - Delay in providing the result of the CSF analysis of the lumbar puncture

Diagnostic thought process

- Perception
  - Where the diagnosis begins
- Hypothesis generation
  - Heuristics: process of establishing a diagnosis by intelligent guesswork
    - Representative: thinking is overly influenced by what is typically true
    - Availability: a cognitive overemphasis on things coming to mind easily

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Diagnostic thought process

- Data interpretation
  - Adjusting the hypothesis by using test results
- Verification
  - Overconfidence: physicians can be poor at assessing the gaps in their knowledge, tending to overestimate both how much, and how reliably they "know" a subject
  - Confirmation bias: the tendency to seek out, notice and remember whatever information fits best with one's pre-established expectations

Graber, ML, et al. “Reducing Diagnostic Errors in Medicine: What’s the Goal?” *Academic Medicine.* 2002, Vol 77, 981-992.

How can we reduce diagnostic errors?

- Continued knowledge advancement
- Earlier disease detection
- Avoid “tunnel vision” by avoiding biased judgment
- Developing a broad differential
- Consult specialists if needed
- Understand the pitfalls of heuristics

Graber, M, et al. “Reducing Diagnostic Errors in Medicine” *Academic Medicine.* 2002, Vol 77, 981-992.

Croskerry, P. “The Importance of Cognitive Errors in Diagnosis and Strategies to Minimize Them.” *Academic Medicine.* 2003, Vol 78, 775-780.

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Important learning points

- Clinicians should not delay or forget lumbar puncture as a diagnostic tool
  - In any patient with unexplained mental status changes
  - Even if there are no fever or meningeal signs
  - Even if there are other possible reasons for mental status changes that are unconfirmed

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