CLINICAL PRACTICE

Exercises in Clinical Reasoning

Anchors Away

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KEY WORDS: anchoring bias; cognitive load; base rate neglect; heuristics; confirmation bias; sore throat.

J Gen Intern Med 29(10):1414–8

DOI: 10.1007/s11606-014-2879-9

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In this series, a clinician extemporaneously discusses the diagnostic approach (regular text) to sequentially presented clinical information (bold). Additional commentary on the diagnostic reasoning process (*italic*) is interspersed throughout the discussion.

A 21-year-old college student presented to the Emergency Department with a 5-day history of sore throat, fatigue, and fevers.

Sore throat is a common clinical complaint in practice. The most likely etiologies are garden variety infections including viruses and strep throat. In a college student, I would consider Epstein-Barr virus (EBV) infection or mononucleosis as well as acute human immunodeficiency virus (HIV) infection, which often presents with sore throat and fever. Gonorrhea is also a possibility, so I would want to explore his sexual history, in addition to learning more about the time course and associated symptoms. In terms of non-infectious etiologies, we should also consider a hematologic malignancy such as lymphoma or leukemia, but this would be much less likely.

Clinical problem solving (CPS) case discussions may provide insight into how diagnostic experts approach complicated cases in actual practice. However, CPS norms and audience expectations often oblige the discussant to demonstrate a broad differential diagnosis and erudition (i.e., an analytic approach) that may not reflect typical clinicians' cognitive tendencies. The limitations of working memory have led to evolutionary pressures on the brain to minimize its work load by using non-analytic reasoning, or pattern recognition, as the default problem-solving strategy. The literature suggests that clinicians approach most problems using non-analytic reasoning, first considering the most likely diagnosis, and then considering alternatives only if the initial diagnosis proves inadequate. Similarly, this discussant first uses pattern recognition for a young adult with sore throat to develop his differential for the most

likely etiologies. The discussant then follows the traditional CPS model by highlighting multiple possibilities, even unlikely ones. This commonly utilized CPS approach may be thought of as "anti-heuristic." A heuristic is a non-analytic mental shortcut that improves problem solving efficiency. In this case, the discussant may be thinking, "CPS exercises are usually complicated, so I should use analytic reasoning to avoid falling prey to biases or heuristics."

The patient was in his usual state of good health until 5 days earlier, when he woke up with a severe sore throat and fevers to 101 °F. Generalized weakness and fatigue developed, and he spent the next several days in bed. He reported dizziness upon standing and intermittent severe headaches, but no neck stiffness or photophobia. He felt slightly winded, even at rest, and noted a pain in his chest when taking a deep breath. He developed a mild dry cough the day prior to presentation.

We learn that the sore throat is severe and that he has associated headaches, dyspnea and orthostatic symptoms—all implying that he is fairly sick. The acuity of his illness and fever suggest that the most likely underlying etiology is an infection. It is difficult to narrow the differential diagnosis with respect to infections except to keep in mind that the likelihood of Group A streptococcal pharyngitis is diminished by the presence of cough, but enhanced by certain physical findings such as fever and tonsillar exudates. The symptoms of cough, dyspnea, and pleuritic chest pain imply a lower respiratory infection or pneumonia such as that caused by pneumococcus (although that infection would be less likely to present with sore throat). However, certain viruses, including herpes simplex, adenovirus, or influenza, may present with both pharyngitis and pneumonia, especially in an immune-compromised host. I still favor a viral infection as being most likely—that is, a less common clinical manifestation of an extremely common infection.

As more data emerge, the discussant naturally falls into non-analytic thinking. He alludes to a clinical prediction rule for sore throat,¹ but notes that the patient's presentation does not fit the typical story or illness script for Group A streptococcal pharyngitis. Despite an initially broad differential diagnosis, the discussant remains anchored on a viral etiology, the first hypothesis raised in his discussion. Anchoring is a well-known cognitive phenomenon where an

Published online May 20, 2014

initial hypothesis or piece of information holds significant sway over thinking to such an extent that subsequent supportive data may be overvalued while refuting data are undervalued. Anchoring may enhance or worsen diagnostic performance, depending on whether the clinician anchors on the correct hypotheses and data. In this case, the discussant continues to “favor a viral infection”, despite the possibility of a potentially more dangerous bacterial infection.

The patient had no significant past medical history and his only medication was acetaminophen for fevers. He was born in the US and of Hmong descent. He lived in a college dormitory and volunteered regularly at a skilled nursing facility. He reported recent family visits to Fresno, California, but denied other travel. He drank alcohol at parties, up to five beers per night, but did not smoke or use illicit drugs. He was sexually active with women and reported two new partners in the last year.

Living in the dorms puts him at risk for mononucleosis, which could cause a severe pharyngitis, although I would also consider meningococcemia due to the acuity and systemic nature of his presentation (possibly shock) and severe headache. Although coccidioidomycosis is an intriguing possibility due to frequent travel to the California Central Valley, he appears too sick for this infection. Any sexually active adult is at risk for HIV and its associated opportunistic infections including pneumocystis pneumonia.

The discussant’s commentary highlights the challenges placed on working memory in a complicated case when analytic reasoning is the primary modality of problem solving. Considering the hard-wired ability of short-term memory to hold roughly seven pieces of data at once, we note the discussant has multiple symptoms (e.g., fever, sore throat, and pleuritic chest pain) and epidemiological features (e.g., dormitory living, travel exposure, sexual history) to process. As the clinician reaches the limits of working memory, the potential for error increases. The cognitive psychology literature calls this type of brain strain, “cognitive load.”² Combining multiple data pieces under a category (“chunking”) provides one means of reducing cognitive load. With experience, experts chunk risk factors, symptoms, signs, and other data into disease categories to minimize the amount of data kept in working memory. In this case, when the discussant thinks about viral infection as a broad category on his differential diagnosis, he likely “chunks” together symptoms like fever, sore throat, dyspnea, and headache to reduce cognitive load.

In the Emergency Department, vital signs were temperature 101.9 °F, heart rate 113, blood pressure 94/43, respiratory rate 24, and oxygen saturation 94 % on room air. On physical examination, the patient appeared ill and diaphoretic. He had dry mucous membranes and his tonsils were enlarged and erythematous without exudates. His tympanic membranes were

normal. He had tender cervical lymphadenopathy that was more prominent on the right side. His neck was supple. Heart was tachycardic but regular and without murmurs. Lungs had fine bibasilar crackles. Abdomen was benign. There were no skin rashes or lesions.

The most prominent physical findings are fever, hypotension, non-exudative pharyngitis and rales, a clinical picture most consistent with pneumonia causing the systemic inflammatory response syndrome (SIRS). In terms of specific etiologies for pneumonia, I favor the following: influenza or other viruses associated with pharyngitis such as EBV or cytomegalovirus; pneumococcus because it is extremely common; or possibly an HIV-associated infection such as pneumocystis jirovecii. Although pneumococcal pneumonia and pneumocystis would account for fevers and pulmonary symptoms, they are unlikely to cause pharyngitis. I would order a chest film, complete blood count, blood cultures, HIV serology, nasal swab for influenza, throat culture, and heterophile antibody test.

The discussant focuses on the updated key features of the patient’s presentation, sharpening his problem representation. However, he continues to anchor on viral causes, as evidenced by the first three diagnoses on his list. Although viruses may cause SIRS, bacterial infections are more commonly incriminated. It seems that the initial framing of the case as sore throat and fever continues to have a strong influence on his reasoning. Anchoring often causes base-rate neglect: when a hypothesis or diagnosis becomes entrenched in a clinician’s mind, the actual prevalence (i.e., base-rate) of the disease is neglected. In this case, the presence of SIRS physiology should shift the discussant more strongly toward bacterial processes.

The white blood cell count was 10,000/mm³, hemoglobin 11 g/dL, and platelet count was 61,000/mm³. The serum sodium was 133 mEq/L, potassium 3.3 mEq/L, chloride 103 mEq/L, and bicarbonate 24 mEq/L. The blood urea nitrogen level was 16 mg/dL and the creatinine 1.02 mg/dL. Alkaline phosphatase was 94 U/L, AST 60 U/L, ALT 65 U/L, total bilirubin 0.8 mg/dL, and INR 1.0. Serum lactate was 1.7 mmol/L. A rapid strep test was negative. Urinalysis was normal. Peripheral smear showed normal sized platelets but a reduced number, and no schistocytes or atypical lymphocytes. An electrocardiogram showed sinus tachycardia. Chest radiograph showed mild cardiomegaly with increased interstitial lung markings.

There is mild elevation in hepatic enzymes and mild lactic acidosis, but the most prominent laboratory finding is thrombocytopenia. Despite absence of schistocytes on the peripheral smear, this is probably due to disseminated intravascular coagulation in the setting of a severe systemic infection, although bone marrow suppression is also possible. In terms of specific causes, a bacterial pneumonia now seems most likely or possibly a viral pathogen associated

with thrombocytopenia and sepsis such as hantavirus. Viral infection could explain the relatively normal white blood cell count. Of course, the pulmonary infiltrates could also represent non-cardiogenic pulmonary edema due to SIRS from any cause. I would definitely begin broad-spectrum antibacterial therapy and volume resuscitation.

The discussant at last ranks bacteria as the most likely causal organism, likely because the severity of illness has become part of his problem representation. However, he seems to have disregarded the atypical features (sore throat and lymphadenopathy) that make bacterial pneumonia less likely. This tendency to focus on data supporting one's hypothesis (e.g., septic picture with respiratory symptoms and signs) and discount information that refute it is called confirmation bias. Cases like this demonstrate the pitfalls of using non-analytic reasoning without a sufficient degree of analytic reasoning to provide confirmatory evidence for one's differential diagnoses.

The patient was admitted for sepsis with a presumed pulmonary source. He was volume resuscitated and started empirically on moxifloxacin and oseltamivir. On hospital day 2, he developed acute abdominal pain in the upper quadrants and left flank pain with continued fevers up to 104.5 °F. On exam the patient appeared toxic, diaphoretic, and in moderate respiratory distress. His abdomen was diffusely tender, most notably in the left upper quadrant with voluntary guarding but no rebound tenderness. There was no costovertebral angle tenderness. White blood cell count increased to 14,000/mm³ and lactate was elevated at 2.9 mmol/L.

The patient is deteriorating rapidly with lactic acidosis and severe left upper quadrant pain, which I cannot readily explain in the setting of acute pneumonia. However, there are very few causes of acute left upper quadrant pain, most notably splenic infarction or embolism, a common complication of endocarditis. In light of his septic picture, I would obtain an urgent abdominal CT scan to look for abscess or metastatic infection.

The patient's dramatic turn for the worse provides further support for a bacterial cause and now opens the door for an alternative diagnosis that would explain the entire clinical picture. Analytical satisfaction with a diagnosis derives from its adequacy, coherence, and parsimony. Adequacy means that the diagnosis accounts for all pertinent positive and negative findings. Coherence refers to the principle that the patient's pathophysiology should fit with known manifestations of the presumptive diagnosis. Parsimony, or Occam's razor, suggests that the simplest solution to a problem is best; thus one (unifying) diagnosis is better than two.³

HIV antibody and viral load, heterophile antibody, and respiratory viral panel all returned negative. On the second hospital day, the admission blood cultures returned positive for anaerobic Gram-negative rods.

Oseltamivir was stopped and antibiotics were changed to piperacillin-tazobactam. CT of the abdomen and pelvis showed no intra-abdominal pathology or abscess. However, there were small to moderate bilateral pleural effusions with associated atelectasis and a 1.3 cm hypodense lesion with a small air focus within the consolidated left posterior lung (Fig. 1).

The patient has gram-negative bacteremia, which surely accounts for his SIRS. When I think about gram-negative organisms causing pharyngitis, I think about *fusobacterium*, especially considering the patient's young age. Hopefully he will improve with changing the antimicrobial regimen, which now includes anaerobic coverage. There appears to be a small lung abscess in the left lower lobe, which could be a manifestation of septic pulmonary emboli. This complication typically presents as a cavitary peripheral infiltrate and could explain his left upper quadrant pain. So I would obtain an echocardiogram to evaluate for endocarditis.

The presence of Gram-negative bacteremia in a young adult with pharyngitis triggers a new diagnostic hypothesis, fusobacterium bacteremia. The discussant has now recognized a familiar pattern—gram-negative pharyngitis—leading him to consider fusobacterium infection. Bacteremia in combination with lung abscess brings to mind septic pulmonary emboli. The discussant uses pathophysiologic reasoning (i.e., an analytic approach) to find support for his new pattern recognition-triggered hypothesis. In complex cases, a careful search for key clues and a combination of non-analytic and analytic reasoning is often required. A hypothesis-driven

Figure 1. A CT scan revealed bilateral pleural effusions with atelectasis. Within the consolidated lung on the left, a 1.3 cm lung abscess is shown (arrow). There was no evidence of intra-abdominal pathology.

approach is preferable to a pan-test or pan-scan approach, because it is more likely to yield a clinically significant finding and is typically more cost-effective.

On hospital day 3, the patient remained persistently febrile and developed worsening right-sided neck pain. On exam he was noted to have a new tender swelling of the right neck just anterior to the angle of the jaw. The submandibular glands were normal and no other neck masses were found. A transthoracic echocardiogram showed a small pericardial effusion but no vegetations.

The patient has worsening neck pain and localized right neck swelling. These findings in combination with gram-negative bacteremia and possible septic pulmonary emboli raise the possibility of a neck abscess or septic thrombophlebitis involving the internal jugular vein. This is a serious endovascular infection that manifests similarly to endocarditis including fevers and embolic phenomena, and may complicate pharyngitis due to *Fusobacterium*. I would obtain a contrast CT of the neck to further evaluate this possibility.

A CT of the neck with contrast showed lack of opacification of the right internal jugular vein with clot (Fig. 2). Blood cultures were speciated as *Fusobacterium necrophorum*.

The patient indeed appears to have septic thrombophlebitis of the internal jugular vein, or Lemierre's syndrome. Such patients typically require prolonged antibiotics and close follow-up. In retrospect, I should have considered this diagnosis much earlier in a patient with pharyngitis and severe systemic illness.

The patient was continued on piperacillin-tazobactam for presumptive Lemierre's disease. He had a prolonged hospital course complicated by multiple septic emboli to the lungs, which later progressed to bilateral empyema requiring chest tube drainage. He eventually completed a 6-week antibiotic course and was successfully discharged home.

DISCUSSION

This case highlights the challenges inherent in the diagnostic reasoning process. In complex cases, a multitude of data must be quickly interpreted for clinical relevance. Evolutionarily, the human brain is designed to seek out patterns to enable rapid decision making. Usually, this non-analytic problem solving approach (pattern recognition) is highly effective and efficient. However, this case illustrates the tendency clinicians have to anchor on their early diagnostic hypotheses. Anchoring can lead to base-rate neglect, the tendency to ignore disease prevalence, and confirmation bias, the tendency to focus on findings that support one's hypothesis while neglecting findings that refute that hypothesis. The latter bias is most concerning from a diagnostic standpoint.

Figure 2. A CT scan of the neck with contrast revealed a complete lack of opacification of the majority of the right internal jugular vein with clot identified (arrow).

The mind has an incredible capability for “selective perception,” a focus on things that seem important in a given mental moment based on a lifetime of experience. Once again, this is essential from an evolutionary perspective. Without selective perception, clinicians would be unable to filter out meaningless data or “red herrings” that can increase cognitive load and prevent correct diagnosis. On the other hand, if clinicians filter out critical data, diagnostic error results. Adding to this challenge is the importance of the initial problem representation.⁴⁻⁷ The discussant initially focused on viral syndromes because the chief complaint was fever and pharyngitis. The differential diagnosis and anchor would have changed significantly had the case been framed as fever, pharyngitis, and hypotension. Thus, this case also illustrates framing bias, a heuristic describing the dramatic effects that subtle changes to the initial presentation have on subsequent clinical problem solving or decision making.

Given the powerful interplay of heuristics and biases inherent in the diagnostic process, what is a clinician to do? The cognitive psychology literature supports the sequential inclusion of non-analytic and analytic reasoning in all cases, even straightforward ones.^{8,9} In this example, it took the blood culture results to lift the discussant's anchor, which was initially fixed on a viral syndrome. Analytic reasoning can serve as a cross-check (e.g., is the diagnosis adequate? coherent? parsimonious?) to confirm that non-analytic reasoning is on the right track.³ When struggling with a difficult case, remember the flight attendant's final words prior to take off – “Cross-check complete” – then perform your own.

CLINICAL TEACHING POINTS

1. Lemierre's syndrome is a serious complication of an acute oropharyngeal infection characterized by septic thrombophlebitis of the internal jugular vein and metastatic infection, typically affecting healthy adolescents and young adults (ages 15-30).^{10,11} *Fusobacterium necrophorum*, a gram-negative anaerobe, is the pathogen responsible for most cases. The disease is potentially fatal without early diagnosis and treatment.
2. In the post-antibiotic era, this disease was referred to as "the forgotten disease" because it was rarely encountered. However, several studies have described a re-emergence of Lemierre's syndrome.^{12,13} The increased incidence may be partially explained by current antimicrobial prescribing patterns, with antibiotics being used more sparingly for sore throat.¹³
3. Although a conservative approach is appropriate for most patients with acute pharyngitis, clinicians should recognize the red flags in young adults with sore throat, including neck pain, unilateral neck swelling, and pulmonary symptoms.^{11,14} If such factors are present, a more aggressive approach is warranted, which includes obtaining blood cultures, imaging to evaluate for internal jugular thrombophlebitis, and initiating early antimicrobial coverage for anaerobes.¹⁵

Acknowledgements: None.

Conflict of Interest Statement: The authors declare that they do not have a conflict of interest.

Funding Source: None.

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