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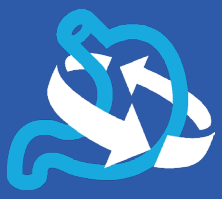

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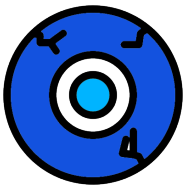
Gastric Volvulus

by:
Stephanie Winslow MD



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Neuromyelitis Optica

by:
Arthur Broadstock MD

GASTRIC VOLVULUS

Stephanie Winslow MD
University of Cincinnati R2

History of Present Illness

The patient is a female in her 50s who presented to the emergency department via helicopter EMS altered with active hematemesis. The patient initially presented to a rural fire station with profuse hematemesis and a chief complaint of abdominal pain. In route the patient became altered and hypotensive leading the transport team to begin transfusing the patient. On arrival to the Shock Resuscitation Unit transfusion of packed red blood cells were ongoing.

Past Medical History

Alcoholic cirrhosis

Past Surgical History

Hysterectomy

Medications

None

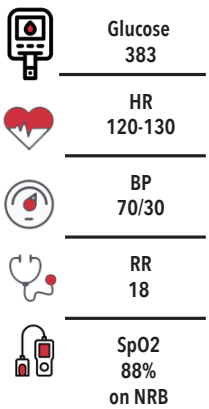
Allergies

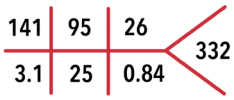
Sulfa antibiotics

Physical Exam

The patient was a cachectic, ill appearing female, with active hematemesis. The patient was tachycardic without other cardiac abnormalities. The abdomen was distended and diffusely tender. The patient spontaneously moved all four extremities but was altered and unable to follow commands. The patient was cool to the touch. The patient's physical exam was otherwise unremarkable.

Diagnostic Tests





Lactic Acid 3.8 INR 1.1
VBG: 7.36/53/+3.5 Troponin <0.04
LFT: Total bilirubin 0.5, Direct bilirubin 0.1, AST 16, ALT 26, ALP 210, Albumin 2.1
FAST examination was adequate and negative.
Portable chest x-ray showed low lung volumes with severely distended bowel loops in the upper abdomen which are incompletely visualized.
Portable abdominal x-ray showed pneumoperitoneum.

Hospital Course

Upon arrival to the emergency department the patient was hypoxic, hypotensive, and tachycardic with active hematemesis. The patient was rapidly intubated and Minnesota tube placement was attempted, given hematemesis in a patient with a known history of alcohol abuse. Minnesota tube placement was ultimately unsuccessful as the tube could not be advanced beyond 20 centimeters. The patient was treated with intravenous pantoprazole, octreotide, ceftriaxone. The patient was transfused a second unit of pRBCs and FFP leading to improvement in her blood pressure. Acute Care Surgery was consulted following evidence of pneumoperitoneum on radiographic studies and patient was taken to the operating room for exploratory laparotomy. The exploratory laparotomy revealed evidence of a gastric volvulus and the patient underwent detorsion of the volvulus, lysis of adhesions, and partial gastrectomy with temporary closure. The following day, the patient returned to the operating room for G-tube and J-tube placement with EGD and closure of the abdomen. The patient was extubated on hospital day 2 and was discharged home to self-care on hospital day 10.

Discussion

Clinical Presentation and Epidemiology

Acute gastric volvulus is an emergent condition resulting from an abnormal rotation of the stomach causing obstruction, ischemia, and potential viscous perforation.[1] The diagnosis of gastric volvulus requires a high level of suspicion from the provider. The classic presentation of acute gastric volvulus is based on Borchardt's triad of severe abdominal pain, retching, and the inability to pass a nasogastric tube.[2] The patient may begin with productive vomiting, but this will often transition to nonproductive retching. There may be blood in the productive emesis if present, which is typically related to mucosal ischemia. This triad has been reported in up to 70% of cases of acute gastric volvulus.[3] Patients additionally often present with hematemesis either from mucosal tearing or mucosal sloughing in the setting of ischemia.[4] Additionally, patients may also present with cardiovascular and respiratory compromise, often sequelae of gastric necrosis and perforation.

Gastric volvulus has a bimodal pattern of incidence, presenting in both pediatric and adult populations. Gastric volvulus presents at a mean age of 24 months within the pediatric population and is commonly associated with anatomic anomalies of the surrounding organs.[5,6] In the adult population, acute gastric volvulus presents in the fifth decade of life with both sexes equally affected. Risk factors for gastric volvulus include abnormalities of the diaphragm (table 1) as well as history of surgery due to the presence

of adhesions.1 The mortality of gastric volvulus is reported to be between 15% to 50%, making early diagnosis and intervention important factors in patient survival.[1,4]

Abnormalities of the Diaphragm
Hiatal/Paraesophageal hernia
Diaphragmatic eventration
Phrenic nerve dysfunction
Kyphoscoliosis

Table 1

Classification

Gastric volvulus can be classified based on the etiology of the rotation. The stomach is fixated within the abdomen by four ligaments: the gastrocolic ligament, the gastrohepatic ligament, the gastrophrenic ligament, and the gastrosplenic ligament. Primary gastric volvulus is due to abnormalities of these ligaments due to adhesions, neoplasia, or laxity of the gastric ligaments.[4] Secondary gastric volvulus is due to abnormality of gastric or nearby organ anatomy, often associated with a paraesophageal hernia or traumatic diaphragmatic injury.[1] Gastric volvulus is also classified by the axis of malrotation. Organo-axial volvulus occurs in the setting of rotation around the axis of the gastroesophageal junction and the pylorus. Typically, primary gastric volvulus is associated with an organoaxial torsion pattern while secondary volvulus tends to present with a mesenteroaxial pattern[7]. This results in an "upside down" appearance of the stomach with the greater curvature in a superior position relative to the lesser curvature of the stomach.[4] Mesenteroaxial volvulus occurs due to rotation around the axis bisecting the greater and lesser curvature of the stomach[1] (See figure 1).[8]

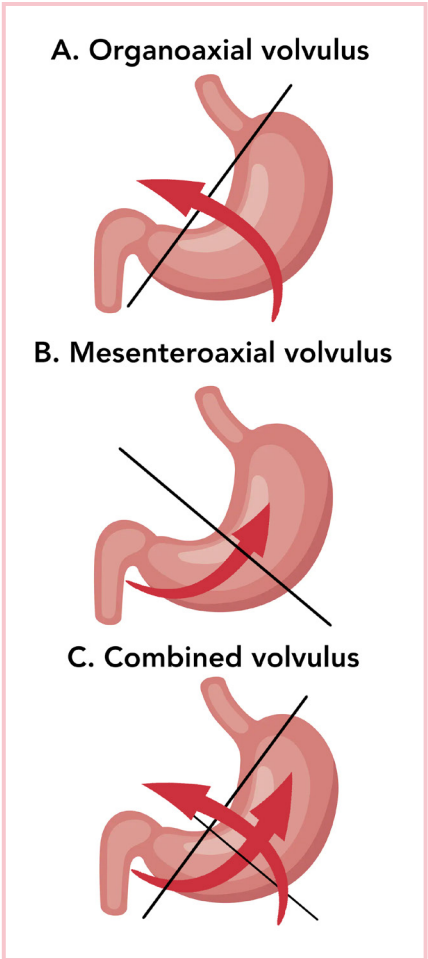


Figure 1: Types of gastric volvulus[13]
A. Organoaxial volvulus results from rotation along the long axis of the stomach from the gastroesophageal junction to the pylorus.
B. Mesenteroaxial rotation occurs with rotation along the transverse axis such that the pylorus rotates above the gastroesophageal junction.
C. Combined volvulus results from a combination of both.

Diagnosis

As acute gastric volvulus can present with nonspecific findings of abdominal pain and retching, the differential diagnosis can be broad and include bleeding esophageal varices and gastric outlet obstruction. Pancreatitis as well as acute coronary syndrome may also be in the differential with upper abdominal pain/lower chest pain and retching. Physical examination can assist in narrowing the diagnostic possibilities. In patients with acute gastric volvulus, the clinician may appreciate upper abdominal fullness and distension in addition to the presence of gastric sounds in the chest on auscultation of the thorax. Failure of attempts to place either orogastric, nasogastric, or Minnesota tubes may also help in making the diagnosis. Radiographic assistance is frequently needed to aid in the diagnosis of gastric volvulus. Indications of this diagnosis on abdominal x-ray include the presence of two air fluid levels in the antrum and fundus of the stomach.[1] If the clinical suspicion is high, but these signs are absent on plain radiographs, then CT imaging is indicated. In a study from in the British Journal of Surgery, barium contrasted studies make the diagnosis of gastric volvulus in 84% (21 out of 25) of patients.[9] However, if the patient is in extremis and barium swallow cannot be performed, plain radiography of the chest and/or abdomen can be performed, understanding that it is less reliable diagnostically. Upper endoscopy is also of diagnostic value in acute gastric volvulus. The benefit of upper endoscopy as a diagnostic test in the setting of suspected gastric volvulus is that it offers both diagnostic and therapeutic potential. Diagnosis of gastric volvulus endoscopically allows for the possibility of endoscopic reduction and fixation with a percutaneous gastrostomy tube during the procedure.[10]

Management

The primary treatment for acute gastric volvulus is surgical intervention. Prior to surgical intervention, attempts to decompress the stomach with a nasogastric tube may be made, but are frequently unsuccessful. Conservative management with nasogastric decompression and monitoring may be an appropriate consideration in hemodynamically stable patients[11]. Patients who are in extremis and show signs of gastric perforation or significant gastrointestinal bleeding should not undergo conservative management.

The operative procedure used to treat the patient's volvulus is guided by the unique underlying cause of each case, with open surgical reduction being the most common procedure performed. Surgical intervention not only includes removal of tissue with evidence of necrosis, but also involves repairing defects to prevent recurrence of the volvulus. Given the increased risk of open surgical procedures, laparoscopic and endoscopic options are an evolving option.[4] A 2016 study by Light et al showed shorter length of hospitalization in patient's undergoing laparoscopic repair of their gastric volvulus compared to patients undergoing an open approach. However, this same study also showed a higher rate of recurrence in patient's undergoing endoscopic management.[12]

Summary

Acute gastric volvulus occurs due to an abnormal rotation of the stomach given gastric ligament or other anatomic abnormalities within the abdomen. Patients typically present with abdominal pain and vomiting due to complications of obstruction, ischemia, or perforation. Plain radiography is the initial test of choice, although CT studies are frequently required. Most patients will require open surgical reduction and fixation; however, initial management should include decompression of the stomach with a nasogastric tube. Laparoscopic and endoscopic options have

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NEUROMYELITIS OPTICA

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History of Present Illness

A female in her 30s with history of diabetes presents with chief complaints of headache, weakness, and dizziness. She reports ten days of symptoms centering around a bilateral occipital headache with associated photophobia. She also reports intermittent diplopia, progressive difficulty with walking, and intermittent vertigo that is not positional or associated with known triggers. She denies fevers, chills, neck pain, nausea, vomiting, numbness, and paresthesias. She is accompanied by her cousin who adds that the patient has also been exhibiting abnormal behavior during this period with intermittent bouts of confusion and inappropriate remarks. Of note, the patient presented to an outside emergency department nine days prior for similar complaints where she had a normal neurologic exam and unremarkable workup that included non-contrasted computed tomography of the head, basic metabolic panel, complete blood count, chest x-ray, EKG, pregnancy test, and urinalysis. She was discharged with ondansetron and meclizine prescriptions, but they have not improved her symptoms.

T
98.6 F

HR
90

BP
123/88

RR
18

SpO2
98%
on RA

Past Medical History
Prediabetes

Past Surgical History
None

Medications
Ondansetron, meclizine

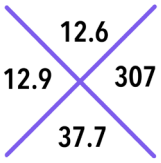
Allergies
None

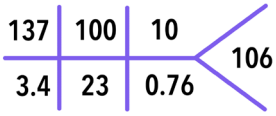
Social History
No alcohol, tobacco, or recreational drug use

Physical exam

Physical exam reveals a female appearing stated age that is alert and interactive, and oriented to person, place, and time. She demonstrates exotropia and a bilateral internuclear ophthalmoplegia, with the remainder of her cranial nerves intact. She exhibits dysmetria in the bilateral lower and upper extremities with truncal ataxia accompanied by an ataxic gait. She is unable to ambulate without assistance. She possesses full strength and intact sensation to light touch in the bilateral upper and lower extremities. She has normal reflexes throughout. There is no meningismus. The patient demonstrates a blunt affect with little insight to her symptoms, laughs inappropriately multiple times during the exam, and exhibits tangential thinking. Auscultation of the heart and lungs is unremarkable. The abdomen is nontender without organomegaly. Examination of the extremities demonstrates strong distal pulses and normal capillary refill.

Diagnostics





Tbili 0.5, Dbili 0.1, AST 30, ALT 49, Alk P 81, Alb 5.1
Urine drug screen is negative
UA: WBC 30, RBC 34, Occasional bacteria
Syphilis Ab: negative
TSH: 2.78

CT Head without Contrast:
Normal

Chest X-ray:
No acute cardiopulmonary abnormality.

MRI Brain:
Faint ring-like area of diffusion restriction within the central midbrain with associated patchy signal abnormality and faint enhancement, with signal abnormality extending inferiorly into the posterior pons. Additional focal area of diffusion restriction with associated patchy enhancement in the medulla. These findings are nonspecific, but differential considerations include a demyelinating process, autoimmune, or toxic-metabolic etiology.

MRI Cervical Spine/Thoracic Spine:
No acute fracture, listhesis, or cord signal abnormality.

Hospital Course

In the ED, despite multiple attempts by the patient to spontaneously void, she ultimately required catheterization, yielding 700 mL of urine. She was given a dose of ceftriaxone in the ED for a suspected urinary tract infection and admitted to neurology due to the concerning MRI findings and physical exam. Broad spectrum antibiotics were discussed with the admitting team, but were deferred due to low clinical suspicion for CNS infection with her initial presentation. A lumbar puncture (LP) was performed that yielded the following results:

Gram stain/Acid fast stain: no organisms
Tube 1: 40,203 RBC, 979 nucleated cells (78% lymphocytes, 9% neutrophils, 4% macrophages)
Tube 4: 5,863 RBC, 688 nucleated cells (73% lymphocytes, 4% neutrophils, 12% macrophages)
West Nile Ag: negative
Enterovirus RNA: negative
HSV 1&2: negative
Lyme IgG, IgM: negative
Autoimmune Encephalopathy panel: negative
IgG: 10.4 (0 – 8.6 mg/dL)
Oligoclonal Bands: 0
Toxoplasma Ab: negative
Cryptococcus Ag: negative

The patient developed an increased temperature on the floor to 100.8 F. While not febrile, given this increased temperature and the elevated cell count with lymphocytic predominance in the CSF, antimicrobials were broadened by the inpatient team to acyclovir, ampicillin, ceftriaxone, and vancomycin. Infectious disease was consulted, and antimicrobials were eventually de-escalated to ampicillin monotherapy for coverage of possible Listeria species after blood and CSF cultures were negative. The patient's mental status progressively declined with worsening somnolence and difficulty following commands requiring transfer to the intensive care unit. On hospital day nine a send out lab for NMO/AQP4 CSF antibodies was positive (1:10). Repeat MRI demonstrated progressing enhancement in the midbrain and medulla relative to the prior study (Figures 1, 2) consistent with neuromyelitis optica in the setting of positive serologies. The patient was intubated for airway protection and high-dose methylprednisolone and plasma exchange were initiated.

Her hospital course was complicated by respiratory failure sec-

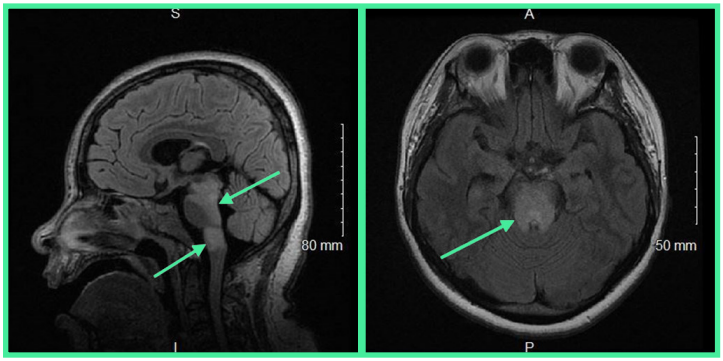


Figure 1 (left): Sagittal T2 FLAIR MRI demonstrating lesions to the pons and midbrain

Figure 2 (right): Axial T2 FLAIR MRI demonstrating lesion to the pons

ondary to Acinetobacter pneumonia as well as Clostridium difficile colitis. Her neurologic course was exacerbated by neurologic storming and intractable vomiting, thought to be secondary to area postrema syndrome. A total of five plasma exchanges were completed without clinical improvement and therefore was started on rituximab infusions. A tracheostomy was performed on hospital day twenty-one. She was discharged to a post-acute care center on hospital day thirty-one in an unresponsive state. Over the next five months, her neurologic status slowly improved with rituximab and high-dose prednisone therapies. She was gradually weaned off the ventilator and her tracheostomy was decannulated. A percutaneous gastrostomy tube was placed due to persistent dysphagia. She was discharged home on day 183 of her admission, able to walk short distances with a walker, minimally verbal, but able to follow commands.

Discussion

Neuromyelitis Optica

Neuromyelitis optica (NMO) is a progressive immune-mediated demyelinating disorder of the central nervous system (CNS) that principally involves the spinal cord and optic nerves. Binding of a disease-specific serum NMO-IgG antibody to the aquaporin-4 (AQP4) channel within the CNS leads to an inflammatory humoral response and complement activation that results in astrocyte damage, secondary oligodendrocyte injury and axonal loss, perivascular lymphocytic infiltration, and vascular proliferation.[1,2] Classically, NMO produces confluent areas of demyelination and necrosis of both gray and white matter of the spinal cord. Previously included within the spectrum of multiple sclerosis, NMO is now a separate disease entity, with its own unique serologic biomarker, imaging and histopathologic findings.

The diagnosis of NMO requires either one of six clinical characteristics (Table 1) with the presence of NMO-IgG antibodies, or two clinical characteristics with MRI findings in the absence of NMO seropositivity.

Six clinical findings of NMO
Optic neuritics
Acute myelitis
Area postrema syndrome
Acute brainstem syndrome
Symptomatic narcolepsy
Symptomatic cerebral syndrome

Table 1

The area postrema is a structure in the brainstem responsible for regulation of blood pressure, detection of potential toxins and foreign substances, and induction of vomiting.[4] Acute brainstem syndrome and symptomatic cerebral syndrome refer to deficits localized to anatomic structures within the brainstem and cerebral cortex with a corresponding lesion on MRI. These syndromes can present with vestibulocerebellar symptoms, autonomic dysfunction, bulbar weakness, hemiplegia, and diplopia.[5] Initial treatment for NMO involves immunosuppression using methylprednisolone 1g/day for 3-5 days with monoclonal antibody immunotherapy and plasma exchange as additional adjuncts. If left untreated, mortality rates are high with older landmark studies reporting mortality rates ranging from 25-50%.[6-8] However, with the advent of novel immunosuppressive agents, recent studies have reported mortality between 7-13%.[9-11] Despite these improvements, morbidity remains significant with 20-30% of patients reporting persistent visual or motor deficits despite treatment.[12]

While ultimately the long-term management of this disease falls outside the purview of emergency medicine, we should possess an awareness of this diagnosis and its presentation given its significant morbidity and mortality. NMO can present with a host of clinical features depending on the location of the lesion. This patient presented with two obvious neurologic deficits on exam that helped cue this diagnosis.

Internuclear Opthalmoparesis

Internuclear ophthalmoparesis (INO) occurs when one eye is unable to adduct past midline on lateral gaze and is accompanied by nystagmus of the abducting eye. This phenomenon is caused by a lesion in the medial longitudinal fasiculus (MLF) in the midbrain, which houses interneuronal pathways of cranial nerves II, III, IV, and VI that coordinate horizontal eye movement. The most common cause for an INO is multiple sclerosis, which accounts for approximately 70% of cases, and presents bilaterally in 73% of cases.[13] Another common cause of INO, especially in older patients, is ischemic infarction.[14] This presentation most commonly results from a small arterial occlusion of the penetrating

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CAPSULAR WARNING SYNDROME

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History of Present Illness

The patient was a Nepalese speaking male in his 40s who presents to the emergency department with a chief complaint of left sided weakness. The patient's daughter reported that the last known well time was eight hours prior to arrival. The patient had fallen upon awakening, revealing his left sided weakness. The patient denied headache, vision changes, neck pain, fever, or any other injuries. The patient had no significant past medical history and was not on any anticoagulation or antiplatelet therapy.

Past Medical History
None

Past Surgical History
Ankle surgery

Medications
None

Allergies
None

Social History
Quit smoking 7 years ago

T
98.3 F

HR
110

BP
119/86

RR
16

SpO2
98% via RA

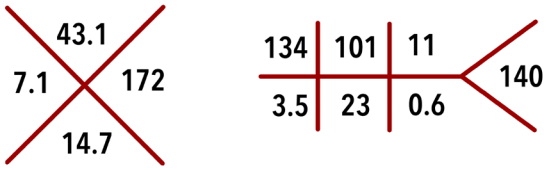
Physical exam

On arrival the patient was well appearing with weakness to the left half of his body. His pupils were equal, round, and reactive to light bilaterally. The patient was alert and oriented to person, place and the date. The patient did not have difficulty with word finding or word articulation. Visual fields were normal in all quadrants. Cranial nerves two through twelve were tested individually and were intact. The patient had full strength on the right side but was only anti-gravity on the left sided (upper and lower extremity). Sensation was intact bilaterally to pain and light touch. The patient had no clonus. Plantar reflexes were downward bilaterally. Finger-to-nose and heel-to-shin test were normal on the right.

National Institutes of Health Stroke Scale on arrival: 7
1a Level of consciousness: 1=not alert but arousable by minor stimulation to obey, answer or respond
4. Facial Palsy: 2=Partial paralysis (total or near total paralysis of the lower face)
5a. Motor left arm: 2=Some effort against gravity
6a. motor left leg: 2=Some effort against gravity, limb cannot get to or maintain (if cured) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity

Notable Diagnostics

CT WO Contrast: No acute intracranial hemorrhage or mass effect.
CTA Head: No acute occlusion or aneurysm.
Chest X-Ray: No acute cardiopulmonary abnormality.



PT 14.8, INR 1.1, APTT 33.2
Troponin I <0.04
BNP 10

Discussion

Hospital Course

The patient was taken immediately to the CT scanner on arrival due to high concern for a possible stroke.While the patient was undergoing non-contrast head CT he had complete resolution of his left-sided hemiplegia and facial droop.

Due to the complete resolution of the patient's symptoms his presentation was thought to be most consistent with transient ischemic attack (TIA). Basic laboratory evaluation was conducted, and Neurology was consulted for admission and evaluation for TIA.

While being evaluated by the neurology team the patient had recurrence of his symptoms with an associated onset of chest pain. Given the recurrence of symptoms in the presence of chest pain, he was taken immediately for a repeat CT of the head and aorta. At the time of his repeat scan his NIH stroke scale was 7 for the same deficits previously stated. The CT head was unchanged, and the CTA of the aorta showed no evidence of dissection.

Given the severity of his symptoms, the neurology inpatient team, stroke team consultant and emergency department physician collaborated deciding to give the patient tissue plasminogen activator (tPA). Consent for tPA was obtained from the patient and his daughter via a Nepalese interpreter as it veered from standard tPA indications. The patient was subsequently admitted to Neuroscience Intensive Care Unit (NSICU) for post tPA care and further TIA/Stroke evaluation.

Upon admission to the NSICU his NIH stroke scale was noted to be five. He underwent a brain MR imaging revealing an "acute

infarction of the right caudate and putamen, in the distribution of the right lateral lenticulostriate artery." He remained stable in the NSICU and 24-hour CT scan demonstrated no bleeding and he was transferred to the neurology floor. While on the Neurology floor he had a fluctuating exam with dramatic motor changes and worsening deficits. A repeat head CT scan showed interval evolution of the ischemic territory involving the right putamen, caudate and internal capsule.

After the initial three days the patient's neurologic exam stabilized. In an effort to identify the cause for his ischemic stroke he underwent a coagulopathy evaluation that was unremarkable. He also underwent transthoracic and transesophageal echocardiography with no significant findings or cause for ischemic strokes. Over the course of the patients seven-day admission his left-sided deficits improved but significant left-sided weakness remained present at discharge. He was discharged to in-patient rehabilitation under the care of Physical Therapy and Physical Medicine and Rehabilitation.

Discharge diagnosis: Right basal ganglia ischemic stroke with left sided spastic hemiparesis and left sided hemineglect.

Discussion

This patient's presentation and course are consistent with Capsular Warning Syndrome (CWS). There is limited understanding of CWS as the majority of literature is limited to case reports, case series, or retrospective analyses. CWS is suggestive of an impending lacunar infarct of the internal capsule. The affected arteries in CWS are classically the lenticulostriate arteries, within the internal capsule (figure 1), which are thought to be damaged by lipohyalinosis, atherosclerotic changes, or hypoperfusion.[1-3]

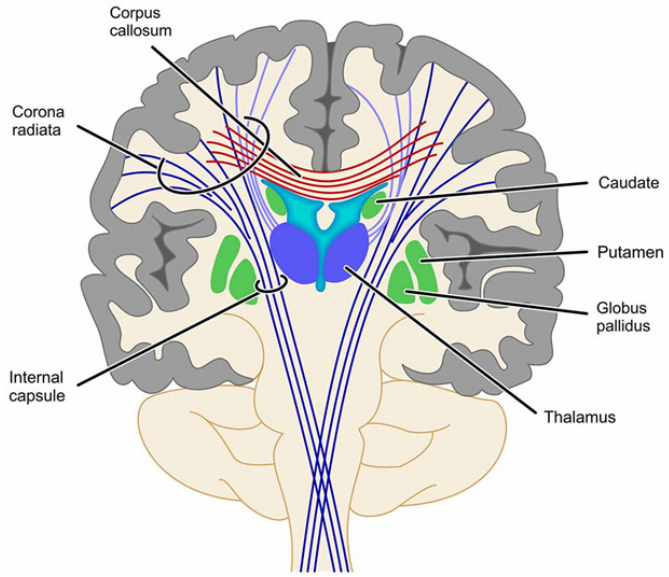


Figure 1: Localization of internal capsule

Original Description & Criteria

The constellation of symptoms which make up this syndrome was initially described in the Neurology literature of 1993.[4] Its recognition was due to observing repetitive stereotyped presentations of patients with recurrent TIA who rapidly progressed to infarctions. In the initial description, a patient needed to have three or more episodes of neurologic deficits with complete resolution within 24 hours to meet criteria for CWS. The neurologic deficits in the initial description of the condition were almost exclusively unilateral face, arm, and leg motor deficits though some had combined sensory and motor deficits.

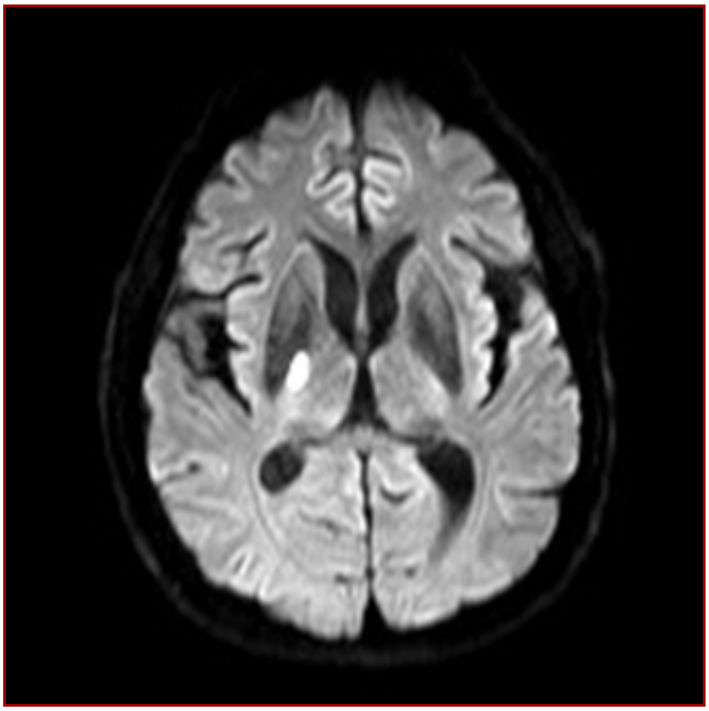


Figure 2: Infarct of the posterior limb of the internal capsule[15]

Clinical Presentation

When patients present with CWS they will typically have isolated motor symptoms and on average will experience five TIA-like episodes before progressing to an ischemic stroke.[5] This typical presentation has continued to be born out in many case reports, yet other causes of the syndrome have been identified including vascular damage or large vessel disease.[6-8] Atypical presentations involving sensory symptoms have also been reported.[9] Some authors have suggested that the term CWS be changed to "Vascular Warning Syndrome" as modern imaging has revealed this syndrome can occur in small vessels outside of the internal capsule affecting various parts of the corticospinal tract up to 50% of the time.[10]

Diagnostic Criteria and Outcomes

The most recent prospective cohort of patients with TIAs shows that 1.5% of patients met criteria of CWS. This criterion is defined as at least three episodes, lasting approximately 20 minutes complete recovery between episodes, of motor or sensory lacunar syndromes within a 24-48 hour period.[11-12] The urgency in identifying CWS lies in the fact that 60% of patients with CWS have been shown to progress to an ischemic stroke within seven days. This rate is dramatically higher than other patients with TIAs that had an ischemic stroke rate of 10%.[11] Long-term outcomes for these patients generally show modified Rankin scores of less than or equal to 2 in nearly 80% of patients indicating minimal disability.[5,12] Further identification of these patients can be aided by MR diffusion weighted imaging which will most often reflect infarction of the internal capsule (figure 2).

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TYPHOID FEVER

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History of Present Illness

The patient was a female in her mid-20s who presents with fevers, chills, myalgias, and malaise for the past seven days after returning from a month-long trip to India. She completed her malaria prophylaxis, doxycycline, throughout the duration of her trip. She had daily fevers with a maximum temperature of 103 degrees Fahrenheit, which transiently resolved after taking acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs). She visited an urgent care two times prior to this emergency department (ED) presentation and completed a course of azithromycin prescribed for a presumptive ear infection. The patient was taking Atovaquone-Proguanil, at this presentation, which was prescribed during the second urgent care visit for presumptive malaria. She denied cough, hemoptysis, abdominal pain, nausea, vomiting, diarrhea, rash, joint pain, or neck stiffness. She was up to date on her immunizations. Travel history included visiting western India, including an area with endemic malaria and dengue. She denied sick contacts or farm animal contacts.

Past Medical History, Medications, Allergies

None

Social History

Nonsmoker
No drug or alcohol use
Married, sexually active with one male partner

Physical Exam

T 99.1
HR 86
BP 118/71
RR 11
SpO2 99% on RA

The patient was a well-appearing female. She had moist mucous membranes with no tonsillar exudates or scleral icterus. No cervical or submandibular lymphadenopathy was appreciated. The neck was supple with full range of motion. Auscultation of the heart and lungs was unremarkable. Her abdomen was soft and non-tender with no hepatosplenomegaly or costovertebral angle tenderness. The lower extremities were symmetrical and without edema. Her distal pulses were intact, and there were no obvious rashes, lesions, petechiae, or purpura.

Notable Diagnostics

Complete blood count, basic metabolic panel, liver function tests, urinalysis, pregnancy test, and chest X-ray were unremarkable.

Pre-Hospital Course

Per her outpatient course, the patient had a second urgent care visit after her fevers persisted despite antibiotic treatment with azithromycin. A broad infectious work up had been initiated at that time, including a complete blood count, renal panel, hepatic panel, quantiferon gold test, HIV, hepatitis serologies, serum tests for Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV) antibodies, blood cultures, a urinalysis with culture, and thick and thin parasite smears. She was instructed to continue her antimalarial medication and follow up with infectious diseases (ID) clinic within one week. She had presented to the ED after her PCP notified her of a positive blood culture growing gram negative rods. The rest of her blood work was negative.

Hospital Course

Shortly upon arrival to the ED, she was started on ceftriaxone to cover for suspected Salmonella serotype Typhi infection, which ultimately speciated from the positive blood culture. The patient was diagnosed with typhoid fever, and transitioned her to oral ciprofloxacin for ten days. The patient was discharged on hospital day two with close follow up in ID clinic. At the time of her outpatient ID visit, the patient reported adherence to the antibiotics and had improvement in her fevers and myalgias.

Discussion

Epidemiology and Pathophysiology

Typhoid fever, also known as enteric fever, is endemic in areas with overcrowding and lack of access to water sanitation, with over twenty-one million cases occurring worldwide each year (Figure 1).[1] It is also a significant cause of global mortality, causing approximately 200,000 deaths annually.[1] Typhoid fever has a particularly high incidence rate in Africa, South-central Asia and Southeast Asia. The United States (U.S.), reports approximately 400 cases of typhoid fever annually.[2] In the U.S., typhoid fever is most commonly seen in immigrants or those with recent travel abroad.[2,3] The ability of humans to become asymptomatic chronic carriers of the bacteria makes human-to-human transmission difficult to track and can lead to quick-spreading outbreaks across the globe.[1] Gallbladder disease is a major risk factor for chronic carrier status, as famously demonstrated by Mary Mallon, commonly identified as Typhoid Mary, who was the first asymptomatic carrier identified in the U.S.. Her work preparing food as a cook led to multiple typhoid fever outbreaks prior to her arrest and quarantine in 1907.[4]

Typhoid fever is an infection caused by the gram-negative bacteria Salmonella enterica subspecies enterica that has two different serotypes: Typhi (S. Typhi) and Paratyphi (S. Paratyphi).[5] Typhoid fever is spread through fecal-oral contamination, and illness severity depends on the number of S. Typhi or S. Paratyphi organisms ingested, with higher bacterial inoculation causing more rapid and severe symptom onset.[2,6] Gastric acidity is a key host defense against typhoid infection, and use of antacid medications increases risk of disease transmission.[3] Microorganisms that are not destroyed by stomach acid move into the small bowel and adhere to Peyers patches in the distal ileum. They then invade the lymphatic and systemic circulations where they continue to multiply during

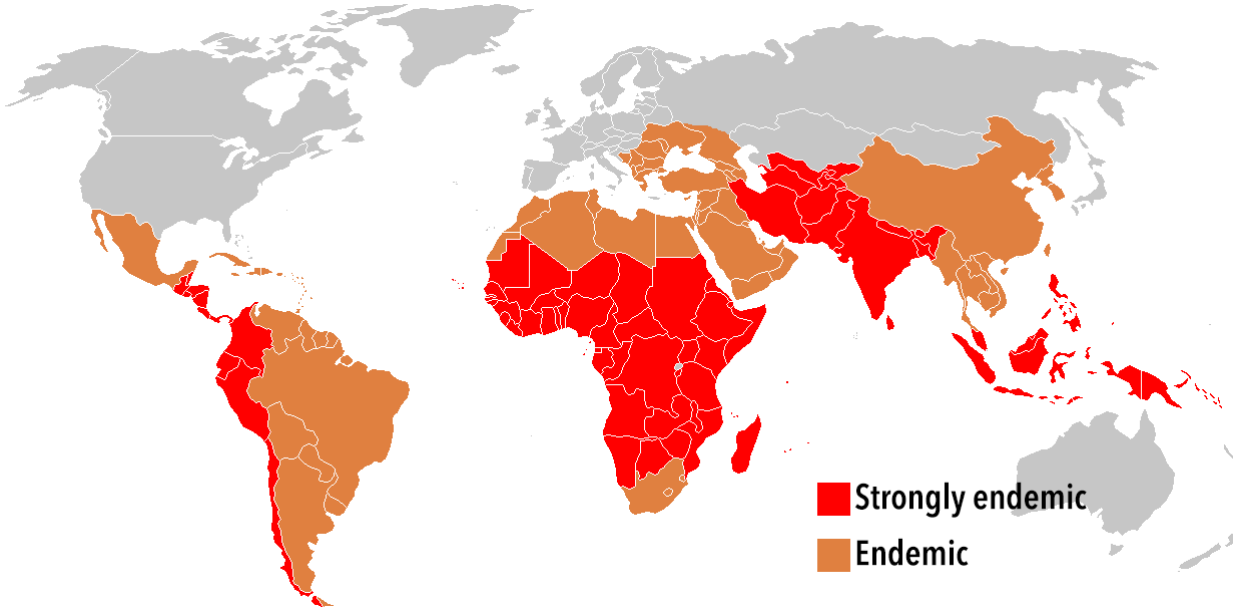

Figure 1: Estimated incidence of typhoid and paratyphoid fevers by country[1]

the one- to three-week incubation period. After the incubation period, the bacteria reenter the bloodstream and distribute to the gallbladder, liver, spleen, and bone marrow where they replicate before returning to the intestinal tract.[3,5,7]

Clinical Presentation

The classic typhoid fever presentation involves an incubation period followed by fevers and nonspecific constitutional symptoms, with both serotypes conferring similar symptoms and prognosis.[5] The incubation period from ingestion to fever onset is between one and three weeks, followed classically by a slow, stepwise rise in fever with a high temperature plateau of 104 degrees Fahrenheit or greater (Figure 2).[8]

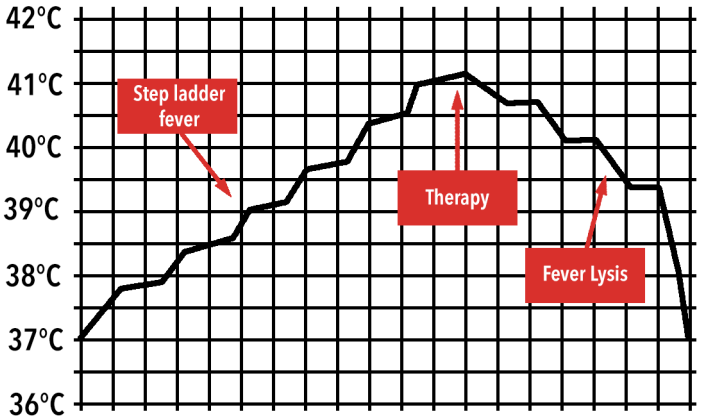

Figure 2: Stepwise fever progression in typhoid fever[8]

Patients frequently have a relative bradycardia (heart rate of less than 80 beats per minute) despite presenting with sustained fever, which is a unique physiologic process known as Faget's sign.[9] Abdominal pain and headache are documented to be the second and third most common symptoms, respectively, along with cough, chills and malaise.[10] Constipation is a common abdominal complaint in adults, thought to be secondary to inflammation and hypertrophy of Peyer's patches causing bowel narrowing and obstruction.[5] In contrast, pediatric patients are more likely to develop diarrhea.[5,7] Children are also more likely to develop febrile seizures and pulmonary manifestations of disease, such as pneumonia.[5,7]

As the disease progresses into more severe stages, patients with typhoid fever may develop hepatosplenomegaly with transaminitis, or a truncal rose-colored macular rash (Figure 3)[3] that is present in one out of every three infected patients. In up to five percent of cases, the inflammation of Peyer's patches leads to gastrointestinal perforation and severe hemorrhage.[10] Intestinal perforation due to typhoid infection is a diagnosis that mimics appendicitis in endemic regions. Rarely, the disease may also lead to central nervous system complications, commonly known as "typhoid encephalopathy," with symptoms ranging from lethargy, psychosis, delirium, stupor and obtundation. Onset of neurologic sequelae typically portends a mortality rate of up to fifty-five percent and is associated with a poor prognosis.[7]

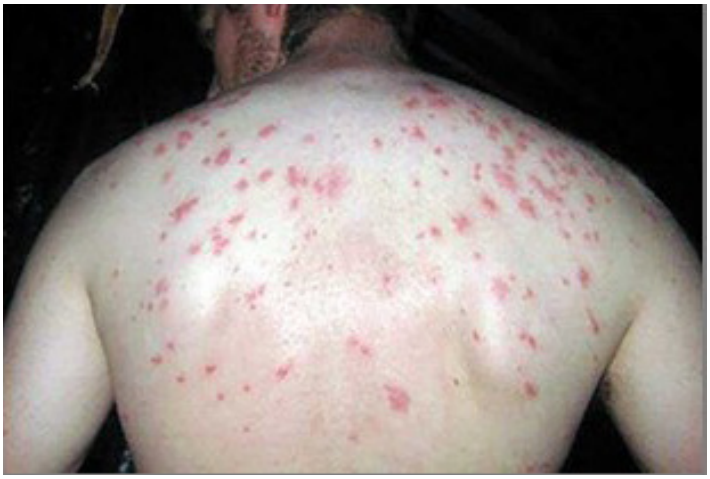

Figure 3: Truncal macular rash seen in typhoid fever patients[3]

Differential Diagnosis

Diagnosing the cause of fever in the returning traveler, such as typhoid fever, is challenging given the vague nature of presenting symptoms, the fact that many tropical diseases are co-endemic in the same regions, and that these disease processes are largely clinical diagnoses without definitive laboratory testing. Furthermore, emergency physicians may have limited training and exposure to these diseases, with studies suggesting that up to forty percent of

Typhoid Fever
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EXTRAPULMONARY TUBERCULOSIS

Colleen Laurence, MD
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History of Present Illness

A female in her 20s with a past medical history of human immunodeficiency virus (HIV), not on antiretroviral treatment, presents to a tertiary hospital emergency department in Uganda with progressive shortness of breath, abdominal pain, and distension for the past two months.

Past Medical History

HIV

Past Social History, Surgical History, Medications, Allergies

None

Physical Exam

The patient is in no acute distress. Breath sounds are diminished on the right, and she appears mildly dyspneic but is able to speak in complete sentences. Her abdomen is soft and large with a fluid wave and tenderness to palpation in the left upper quadrant.

99.6 F	HR 92	136/86	RR 18	91% on RA

Hospital Course

Given the high prevalence of HIV and Tuberculosis (TB) co-infection in the region, you secure a sputum sample for culture as well as a chest x-ray. The sputum culture will take at least 2 weeks to speciate. The chest x-ray reveals a right-sided pleural effusion but no obvious opacifications in the upper lobes or hilar adenopathy suggestive of primary pulmonary TB. Her urine pregnancy test is negative. You do not have access to CT imaging to evaluate her abdominal pain and distension. After discussing your suspicions with your Ugandan colleagues, you decide to perform a Focused Assessment with Sonography for HIV-associated Tuberculosis (FASH).

A FASH exam confirms a right sided pleural effusion with non-complex, hypoechoic fluid as well as paraaortal lymphadenopathy (Figure 2) and multiple splenic lesions measuring between 0.5-1 cm consistent with splenic microabscesses. She is admitted to the general medical ward at the hospital. The patient is initiated on empiric treatment for TB with Rifampicin, Isoniazid, Pyazinamide, and Ethambutol while awaiting sputum culture results and, at time of discharge, is scheduled to follow up with the HIV clinic to discuss initiation of HIV antiretroviral treatment.

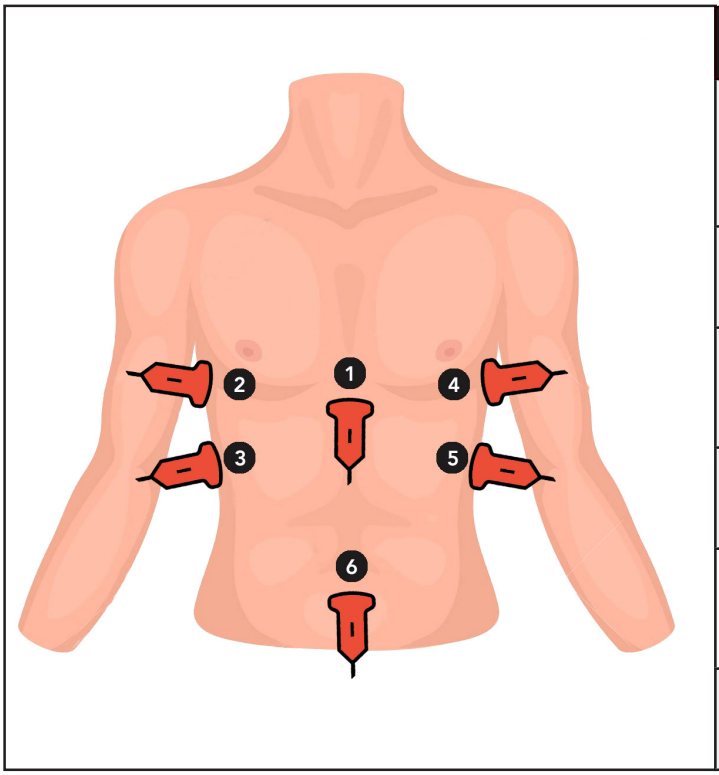
Focused Assessment with Sonography for HIV-associated Tuberculosis (FASH)

The FASH exam was developed to help diagnose extrapulmonary tuberculosis (EPTB) in resource-limited settings where the diagnosis of TB is limited by the low availability of tests. EPTB is commonly seen in immunocompromised patients and is more difficult to diagnose than pulmonary TB. Many resource limited settings lack testing capabilities necessary to diagnose EPTB. In sub-Saharan African almost 20% (19%) of patients with TB have EPTB. In resource-limited settings EPTB is often diagnosed based on WHO case definitions. In the United States the gold standard for diagnosis of EPTB is evidence of caseating granulomas on histology biopsy. Diagnostic challenges are further compounded in individuals with HIV who often present with atypical radiographic findings, sputum negative TB, and extrapulmonary manifestations. These difficulties contribute to diagnostic uncertainty, delayed therapy, and increased mortality in individuals with HIV. One in three HIV deaths is due to TB.

The FASH protocol encompasses six different probe positions, using a curvilinear transducer, to evaluate for pathologic effusions, enlarged abdominal lymphadenopathy, splenic microabscesses, and focal liver lesions (Figure 1).

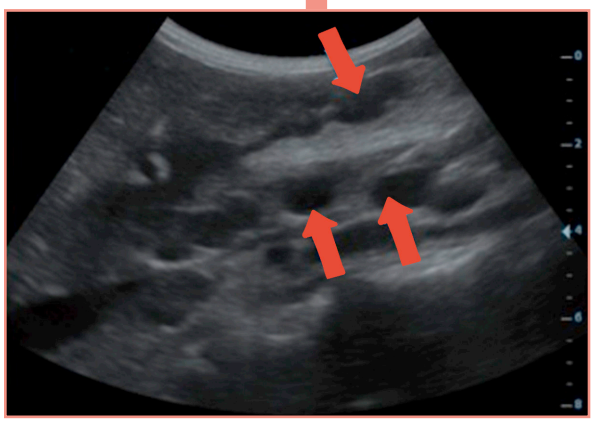
The relative prevalence of pathologic findings discerned on FAST exam varies according to different studies. A retrospective analysis of 82 patients with confirmed abdominal TB from 2013 found enlarged lymphadenopathy in 75.6%, splenic abscesses in 41.2%, and liver lesions in 30.6% of patients. A more recent study found that pericardial effusion was the most common finding in those with confirmed TB, though it was also observed in those categorized as unlikely to have TB (43% v. 10%, $p < 0.001$). Abdominal lymphadenopathy, pleural effusions, and ascites were also common findings in the confirmed TB group and were comparatively rare in the unlikely TB group (24% v. 2% for abdominal LN, $p < 0.001$; 14% v. 1% for pleural effusions, $p< 0.001$; 16% v. 4% for ascites, $p = 0.01$). Abdominal lymphadenopathy followed by pleural and pericardial effusion had the highest positive predictive value and positive likelihood ratio for probable/confirmed TB.

The FASH exam is a useful tool when appropriately applied in high prevalence settings with a large proportion of HIV and TB coinfection. It can be rapidly taught to providers and may change management.1 A positive FASH study increased the likelihood of empiric TB treatment before obtaining other diagnostic studies among those with confirmed TB from 9% (5/56) to 46% (26/56) in one study8 and, in another study, lead to a change in treatment in 72% of patients - most often initiation of TB treatment followed by initiation of ART treatment. While the utility of the FASH exam may not be as high in the United States where there is a relatively low prevalence of HIV and TB coinfection, it offers a systematic and rapid means for evaluating individuals with these comorbidities in low resource settings.



Probe Position: Pathologic Findings
(1) The probe is placed in the transverse axis in the subxiphoid space to evaluate for pericardial effusion, disseminated abdominal lymphadenopathy. Peri-aortic and periportal lymph nodes measuring larger than 1.5 to 2 cm are considered pathologic in an HIV-positive individual.[5]
(2) The probe is positioned posteriorly in the right mid-axillary line to evaluate for a right-sided pleural effusion.
(3) The probe is moved caudally to evaluate for ascites in the hepatorenal pouch and for focal liver lesions. Note: liver lesions may have other infectious etiologies besides TB (eg, amebic disease, echinococcus, schistosomiasis).[3]
(4) The probe is then placed to the left mid-axillary line to similarly evaluate for a left-sided pleural effusion.
(5) Mirroring positioning on the right side, the probe is moved caudally to evaluate for ascites in the splenorenal space and for focal splenic lesions. Splenic lesions often measure anywhere between 0.5 and 1 cm and may represent multiple microabscesses.[1]
(6) Finally, the probe is placed on the lower abdomen in either the longitudinal or transverse axis to evaluate for free fluid.

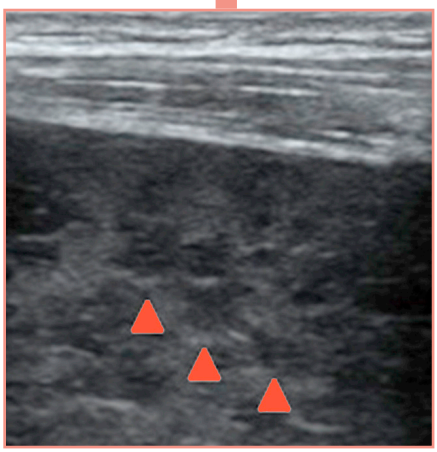
Figure 1: Probe positions and pathologic findings.[5,6]



A

Figure 2

Enlarged para-aortal abdominal lymph nodes, which appear as hypoechoic round structures and are considered pathologic when >1.5 cm, due to abdominal TB are seen as hypoechoic masses (arrows).[9]



B

Figure 2

Multiple hypoechoic microabscesses of the spleen in a patient with disseminated TB (arrowheads).[9]

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Typhoid Fever

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patients presenting with tropical disease infection are improperly diagnosed or treated.[11] However, clarifying onset and characteristics of symptoms, along with specific location of travel and activities completed, can help significantly narrow the differential diagnosis. Thus, providers should consider using the TRAVEL mnemonic to further elucidate key facts regarding the patient's history (Table 1).[12]

Time of onset	Establish incubation period of infection.
Room and board	Mosquito nets, camping, sick contacts.
Activities	Fresh or saltwater swimming, barefoot in sand or soil, insects/animals, sexual activity.
Vaccination and prophylaxis	Specific immunizations for travel area, prophylaxis for malaria or other illness
Exposure	Transfusion, injections, or medical care overseas
Location	Specific geography, dates of arrival and departure, urban vs. rural, travel advisories.

Table 1: TRAVEL mnemonic

Typhoid fever often present with symptoms similar to malaria, and these two infections tend to be co-endemic. Constant and increasing high fevers can differentiate typhoid fever from the intermittent daytime fevers seen in malaria.[8] Additionally, effective anti-malarial therapy leads to fever improvement in malarial infection within hours, whereas typhoid fever resolution occurs gradually in the days following antibiotic administration.[8]Malaria remains the most common cause of fever in travelers, and clinicians should strongly consider a diagnosis of malaria until proven otherwise. Table 2 contains a comparison of a few of the most common diseases to highlight significant similarities and differences.[13,14]

	Typhoid Fever	Malaria	Dengue	Hepatitis A
Microorganism	Salmonella enterica	Plasmodium falciparum	Dengue virus	Hepatitis A virus
Vector	Fecal/oral route	Mosquito vector	Mosquito vector	Fecal/oral route
Incubation period	7-21 days	10-15 days	5-14 days	2-6 weeks
Fever pattern	Constant, stepwise increasing	Intermittent rise and fall (daytime)	Initially high, then decreasing (resolves by day 5)	Low grade fever subsides when jaundice appears
Signs and symptoms	Headache Abdominal pain Constipation Cough	Myalgia Headache Jaundice Hepatomegaly	Headache Nausea Vomiting Arthralgia	Abdominal pain Diarrhea Anorexia Jaundice
Laboratory diagnosis	Culture (blood, stool, urine, bone marrow)	Thick and thin blood smear	Arbovirus serology and PCR	Anti-Hepatitis A IgM serology

Table 2: Comparison of common diagnoses in travelers with fever

Diagnostics

In the U.S. typhoid fever is commonly diagnosed with blood cultures; however, the sensitivity of blood culture is relatively poor at approximately sixty percent.[5] The poor sensitivity of blood cultures is likely due to antibiotic exposure during prior health care visits, along with slow-growing bacterial speciation that make take several days to result.[2] Stool culture is another option, but it can be difficult to obtain if patients are presenting with constipation, and sensitivities are poor.[5] Bone marrow culture is the most accurate diagnostic modality,[2,5] but it is a difficult and invasive test to obtain. The Widal test, developed over a century ago, detects agglutinating antibodies against the O and H antigens of S. Typhi. Although studies have demonstrated that sensitivity and specificity for this test are low, it continues to be commonly used in low-resource endemic areas for typhoid fever diagnosis as it is quick, inexpensive, and widely available.[15] Other rapid serologic tests have been studied; however, none are widely commercially available.[5]

Prevention

Since typhoid fever is spread through the fecal-oral route, improved water and sanitation practices greatly reduced transmission of typhoid fever in middle- and high-income countries.[16] Two unconjugated typhoid fever vaccines are approved for use in the United States: the Vi capsular polysaccharide vaccine (Typhim Vi) for intramuscular use and the oral live attenuated vaccine (Vivotif).[2,5,17] Vaccination is recommended for U.S. travelers as prophylaxis prior to visiting endemic areas. The protective efficacy of the vaccines decreases over time, and repeat vaccination is recommended every three or five years for Typhim Vi and Vivotif, respectively, if travelers plan to visit endemic areas.[2,17]

Treatment

Appropriate antibiotic selection is crucial in management of typhoid fever. The most common first-line treatment is with fluoroquinolone antibiotics, usually a ten-day ciprofloxacin regimen.[6] Ceftriaxone and azithromycin are alternative treatment options in areas where resistance to fluoroquinolones is rising, including many Asian countries such as India and Pakistan.[2] Carbapenems are generally reserved for multi-drug resistant strains and severe cases.[18] Chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole are also being used to treat typhoid fever, as recent studies are showing a reversal in prior trends of resistance in certain endemic regions.[5] Because resistance varies based on the geographic areas in which inoculation with typhoid fever occurred, public health resources should be used to help direct therapy if antimicrobial sensitivities are not available.

Patients with encephalopathy due to typhoid fever may benefit from administration of steroids. The most commonly studied therapy is intravenous dexamethasone that is typically initiated alongside the first antibiotic dose.[5,19]

Summary

Typhoid fever is an infectious febrile illness caused by Salmonella enterica subspecies enterica that is endemic in countries with poor sanitation and is a common cause of fever in a returning traveler. Emergency physicians should perform a thorough travel history in all patients presenting with fever and obtain blood cultures if typhoid fever is suspected. Treatment with fluoroquinolones is first line, but antibiotic resistance is common. Consultation with ID and hospital admission is appropriate for patients with severe symptoms.

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NMO

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arteries originating from the basilar artery, or occasionally from the superior cerebellar or posterior cerebral arteries.

Third cranial nerve palsies can be confused with INO given paralysis of adduction associated with weakness of the medial rectus muscle; however, third nerve palsies should also be accompanied by ptosis and pupil dilation which may help distinguish the two entities. Additionally, a pseudo-INO may be observed in patients presenting with myasthenia gravis and Guillain-Barré syndrome, which are not true manifestations of MLF lesions, but may present similarly.[15]

Causes of INO
Infection (meningoencephalitis, syphilis)
Tumors, trauma
Drug intoxications (TCA, phenothiazines, lithium, propranolol, barbiturates)
Progressive supranuclear palsy
Wernicke encephalopathy
Head trauma

Table 2

Ataxia

This patient also presented with truncal ataxia and an ataxic gait. True ataxia stems from dysfunction of the cerebellum, which is composed of midline cerebellar structures and two large cerebellar hemispheres.[16,17] Damage to midline cerebellar structures can yield an ataxic gait, truncal ataxia, dysmetria, and nystagmus. An ataxic gait is best elucidated with evaluation of tandem gait, and imbalance from midline lesions will be observed when the patient stands with feet together, either with eyes open or closed. Truncal ataxia refers to the inability for patients to sit upright without support, and often appears with swaying of the head or trunk in a seated position. Dysmetria refers to the inability to perform movements due to an erroneous estimation of distance, usually demonstrated through finger to nose testing. Damage to the cerebellar hemispheres can produce dysdiadochokinesis, dysmetria, limb ataxia, intention tremor and scanning speech. Dysdiadochokinesis refers to incoordination when performing rapid alternating movements, as demonstrated through rapid pronation and supination of the forearm, or rapid pinching of the thumb and index fingers. Intention tremors are characterized by broad, coarse and low frequency tremors that worsen as the patient approaches a visually guided endpoint. Scanning speech can be viewed as "oral motor ataxia" and refers to deficits in speech coordination and word timing, manifesting as vowel distortions, irregular articulatory breakdowns, equal stress on syllables and excess loudness variations.[18]

The etiology of ataxia varies significantly with the temporality of symptoms. Chronic ataxias that progress over months to years often suggest a genetic (spinocerebellar ataxia, Friedreich ataxia, ataxia-telangiectasia, Wilson disease, mitochondrial disorders) or a slowly progressive neurodegenerative disorder (multiple system atrophy, progressive supranuclear palsy, normal pressure hydrocephalus). Acute ataxias manifest over the course of minutes to days and are often caused by vascular disorders (cerebellar ischemia/hemorrhage), infection, or acute intoxications (alcohol, phencyclidine). This patient presented with subacute ataxia, which is defined as progressing over days to weeks.

Differential Diagnosis of Subacute Ataxia
Atypical infections
Progressive multifocal leukoencephalopathy, prion diseases including Creutzfeldt-Jakob disease, Whipple disease
Iatrogenic pharmacotherapy
Antiepileptics (most commonly phenytoin, but can present with others that possess Na-channel blockade)
Valproic acid with hyperammonemia
Benzodiazepines
Chemotherapies (cytarabine, fluorouracil, asparaginase)
Heavy metals (Mg, Mn, Bi)
Lithium
Zidovudine
Primary or metastatic tumors in or near the posterior fossa
Paraneoplastic disorders
Chronic alcohol abuse
Wernicke's encephalopathy (B1 deficiency)
Chronic Vitamin E or B12 deficiencies
Endocrine disorders: hypothyroidism, hypoparathyroidism
Autoimmune disorders
Systemic syndromes: systemic lupus erythematosus, Behçet syndrome, Sjögren syndrome, sarcoidosis, celiac disease
Primary neurologic: multiple sclerosis, neuromyelitis optica, acute disseminated encephalomyelitis, Miller Fisher syndrome, Bickerstaff encephalitis, GAD antibody-associated ataxia

Table 3

Summary

Ataxia is a common physical exam finding in the emergency department and carries a broad differential diagnosis that can be stratified by the temporality of symptoms. Internuclear ophthalmoparesis reflects lesions to the MLF, which often carry high morbidity. Neuromyelitis Optica is an autoimmune demyelinating disease process that should be on the differential when ataxia, vision deficits, narcolepsy, nausea and vomiting, or brainstem syndromes are apparent.

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Treatment

Given the debilitating nature of capsular infarcts it is not surprising that many patients who present with CWS are initially treated with TPA.[12] Retrospective studies have shown similar efficacy between TPA and antiplatelet agents, but their application is limited due to their sample size and retrospective design. The suggested treatment modalities for CWS seem to focus on thrombolytic therapy or antiplatelet therapy (dual therapy, monotherapy, or GP IIb/IIIa receptor antagonist).[3,5,11,12] Other common stroke interventions such as blood pressure augmentation have not been well discussed beyond the reporting of patients receiving vasopressors to maintain cerebral perfusion.[13]

CWS should be treated as any other kind of ischemic stroke until more robust data is available. A pooled analysis of the CHANCE and POINT trials demonstrated that early initiation of antiplatelet agents may reduce the risk of future ischemic events.[14] Even though there is a paucity of robust data, the benefit of recognizing CWS lies in the ability to identify a patient who is having precipitously recurrent capsular TIAs, treating them, and attempting to prevent progression to a completed ischemic infarct.

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15. Case courtesy of Dr C. Igler, Radiopaedia.org, rID: 42143

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become more common due to the benefit of decreased length of hospitalization, especially in patients who are at high risk for complication from open operative intervention.

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