Name: Mrs. JB
Medical Record #: N24669 **Prepared by:** KF
Date of Birth: 12/12/1942
Date of Presentation: April 17, 2005, 9:16pm
History and Physical Conducted: April 18, 2005 1-3am
Patient's Room: 93

INFORMANTS:
1) Patient and daughter - fair reliability, poor insight
2) Duke Medical Records from Ebrowser
3) DRH Records

PATIENT PROFILE:
This is a 62 yo white female.

CHIEF COMPLAINT:
Headache, nausea, vomiting, and diarhea

HISTORY OF PRESENT ILLNESS:
This 62 yo female with a PMH notable for TTP in 1996 who presents with intermittent dizziness, nausea, vomiting, and diarrhea of about 1 week duration. Over this period of time, she has been unable to take in any significant PO intake without vomiting. Her dizziness and lightheadedness are most notable when she stands up, and she has difficulty maintaining her balance due to this. She also notes that has been very tired for this past week, spending approximately 20 hours per day in bed sleeping. She denies pain, headache, fevers, chills, SOB, chest pain, hematemesis, bloody stool, tarry stool, dysuria, hematuria, and increased bleeding or bruising. The patient is unable to provide further details or further describe her symptoms, and has no idea what might be causing them. She does deny any recent sick contacts, eating any new or abnormal foods, eating any potentially raw meats, and drinking large amounts of tonic water, or anything else that contains quinine.

PAST MEDICAL HISTORY:
1981 – Cessarian section. This was her fourth and final child.

August 1996 – 9 day hospital admission for TTP. Presented with nausea, vomiting, mental status changes, headache, and exertional dyspnea. After ruling out MI, meningitis, hepatic obstruction, renal insufficiency, and collagen vascular disease, the diagnosis of TTP was eventually made. Hospital course included 8 sessions of plasmaphoresis, 4 sessions of hemodialysis, high dose IV steroids, and an open kidney biopsy which was complicated by a right pneumothorax.

September 1996 – Presented to Duke ED with an infected Perma-Cath and hypokalemia.

July 2000 – Presented to Duke ED with acute bronchitis and bilateral otitis media.

January 2001 – Presented to Duke ED after a fall with fractures of the third and fourth metacarpals. The hand was splinted and later casted

December 2002 – Presented to DRH with dizziness and left sided weakness. CT showed two lacunar infarcts at the left basal ganglia, and well as evidence of some old infarcts. The patient was discharged after a four day hospital stay.

August 2003 – Cataract surgery, left eye

October 2003 – Cataract surgery, right eye

January 2004 – Dilation and curettage for postmenopausal bleeding

In addition to these events, the patient has current diagnoses of HTN and hypercholesterolemia. She is unsure if she has CHF. Her baseline creatinine, at the time of her elective D&C in January 2004, was 1.7.

CURRENT MEDICATIONS:
Lasix, 20 mg PO daily
Potassium Chloride, 8 meq PO daily
Atenolol, 50 mg PO daily
Lipitor, 10 mg PO daily
ASA, 81 mg PO daily
Norvasc, 5 mg PO daily
A green "nerve pill" the patient takes to reduce itching

ALLERGIES/SENSITIVITIES:
NKDA

SOCIAL HISTORY:
The patient lives with her husband in an apartment in Durham. The two of them are unable to care for themselves, so the patient's sister and daughter alternate spending days caring for them. She had four grown children. She denies tobacco, alcohol, and drugs, lives with family. She is not sure if she has ever been employed.

HEALTH MAINENANCE:
The patient sees Dr. R as her PCP. She has had at least one mammogram, but it sounds like it has most likely been quite a while ago. Her most recent pap smear is documented as being 3/12/03, and it was normal. She has never had a colonoscopy. She is unsure what immunizations she has had. She does see Dr. Rat least once a year and says she has little difficulty obtaining or taking her medications.

FAMILY HISTORY:

Both of her parents are dead, but she does not remember how old they were when they died. Her father had COPD and coronary artery disease. Mother had diabetes and stoke. One of her siblings has congenital deftness. Another sibling has adult onset diabetes.

REVIEW OF SYSTEMS:

General – The patient denies fevers, chills, fatigue, and decreased appetite. She has been excessively somnolent for the past week, sleeping through nearly the entire day. She has been experiencing a headache, lightheadness, and has had a generalized feeling of dysphoria.

Skin – Patient points out that she has light scratch marks over much of her body where she has been scratching herself. This scratching has been going on for quite some time and is not new in the past week.

HEENT
Eyes – The patient has blurry vision associated with her dizziness when she stands up. Otherwise, denies blurry vision, double vision, and any changes in visual acuity.
Ears – Denies changes or problems in her hearing.
Nose/throat/mouth/teeth – Denies congestion, rhinorhea, sore throat, and dental pain. She also denies any symptoms suggestive of a recent upper respiratory tract infection. Patient snores.

Respiratory – Denies dyspnea and cough.

Cardiovascular – Denies chest pain, palpitations, and peripheral edema.

Breasts – Denies changes, pain, and masses in breasts.

Gastrointestinal – Patient has diarrhea, which she is unable to quantify or quality. She only reports that this diarrhea is brown, is not tarry, and does not contain blood. Patient does not know when her most recent bowel movement was.

Genito-Urinary – Denies dysuria, polyuria, and hematuria. Denies any recent recurrences of menstrual bleeding. Patient is unable to report whether she has urinated today.

Neurologic – Patient reports that she has had a headache for most of the time over the past week. She does not ordinarily have regular headaches. She also reports that she had a stroke a few years ago, and that she has had some left sided weakness, especially in her left leg, ever since this stroke She denies history of seizures. Her daughter denies any recent changes in mental status.

Musculoskeletal – Denies muscle and joint pain.

Endocrine – Denies diabetes. She notes that she has been very thirsty lately, but has been unable to drink water since she throws up everything she takes in.

Hematopoetic – Denies easy bruising and bleeding. Denies any recent bruises or bleeding.

PHYSICAL EXAMINATION:

Vital Signs – temp 36.5°C, BP 159/76, pulse 58, RR 18, 98% on RA, weight 105 kg, height 166 cm, BMI 38

General – Pleasant, obese 62 year old female currently in no apparent distress.

Skin – Several small, nonpalpable purpura on each upper arm. Two medium brown plaques on back with irregular borders – one is 1x1 cm and located at the midline, level of T4. The other is about 2x2 cm and is located 11 cm to the left of the midline at the level of T7. Slight scratch marks on arms and trunk, consistent with history, but of but apparent significance.

Lymph nodes – No periauricular, cervical, supraclavicular, axillary lymphadenectomy.

HEENT – No scleral or sublingual icterus. Oropharynx clear, mucosa moist. Dentition entirely absent.

Neck – Neck supple. Trachea midline. Thyroid gland normal and nontender. No carotid bruits. Difficult to assess for JVD secondary to body habitus.

Chest – Chest symmetric. Lung clear to auscultation bilaterally.

Heart – Normal S1 and S2. Regular rate and rhythm with no rubs, murmurs, or gallops. PMI normal.

Abdomen – Abdomen is protuberant. Soft, nontender, nondistended. Normal bowel sounds. Midline scar from umbilicus to pubus consistent with history of cesarean delivery.

Rectal – Adequate tone, no masses noted, guiac positive.

Extremities Peripheral pulses – 2+ radial pulses bilaterally. 1+ pedis dorsalis, and posterior tibial pulses bilaterally.
Peripheral edema – 1+ edema in lower extremities, symmetric bilaterally.

Musculoskeletal – Normal passive and active ROM in upper and lower extremities. No focal joint inflammation or abnormalities were noted.

Nervous System Mental status – She is alert and oriented x 3, except that she thinks the year is 2008. She has poor insight consistent with a poor level of education (patient does not remember level of

education), but her daughter says that this is her baseline. MMSE 27/30

Cranial nerves – Slight right-sided facial droop, but strength of facial muscles feels symmetric bilaterally. 2-12 intact.

Sensory – Light touch intact to face, UEs, and LEs bilaterally. Position and pinprick in tact to lower extremities.

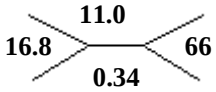
Motor – 5/5 strength in upper and lower extremities. The LLE is slightly weaker than the RLE, but both have very adequate strength. No clonus, no actierctus.

Reflexes – Patellar reflex appropriate bilaterally. Brachioradialis, brachial, and ulnar deep tendon reflexes are all hyperreflexive bilaterally. Babinski positive on right, negative on left.

Cerebellar – Poor finger-to-nose performance.

LABORATORY DATA:

Hematology



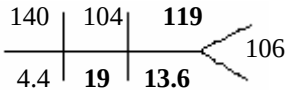
Differential: 71.7% neutrophils (**12.0 total**), 17.6% lymphocytes (2.9 total), 7.1% monocytes, 3.1% eosynophils, 0.5% basophils

MCV 78 RDW-CV 16.8

Peripheral Blood Smear - 5% of RBCs are shistocytes (28 per high power field)
One target-cell seen
Large platelets and clumping of platelets

Reticulocyte Count – 77.8 total, **1.99 % reticulocytes (high)**, **46.0% are immature reticulocytes (high)**

Chem 7



Estimated GFR: 3mL/min

GI –

Other Chemistry - **Ca 7.7**, **Phos 6.7**, total protein 7.3**, albumin 3.6**, **lipase 270**

Lactate dehydrogenase – **3260**

Haptoglobin - <8

RBC IgG - normal

DIC Screen – fibrinogen **460.7 (slightly elevated)**, D-dimer fragments undetectable

Urinalysis – clear yellow; spec grav 1.014; pH 6.0; **3+ protein**; **3+ blood**; **6 rbcs**; **9 wbcs**; **1 hyalin cast**; negative for glucose, ketone, nitrite, leukocyte esterase, and bilirubin; 0.2 urobillinogen; 3 squamous epithelial cells; **5-50 bacteria**

Urine Electrolytes – 94 sodium, 16 potassium, 88 chloride, 50 creatinine. FENA is 18%.

DIAGNOSTIC TESTS:

EKG – nsr, 54 bpm

ASSESSMENT/PLAN:

1) Thrombotic Thrombocytopenic Purpura (Hemolytic Uremic Syndrome)

Diagnostic Pentad:

Microangiopathic hemolytic anemia - This patient has a hemolytic anemia with a significant shistocytosis. The average shishtocytosis in TTP is 8.45% (with a range of 1% to 18%); her shistocytosis was 5%. Her elevated LDH is also confirmatory of her shistocytosis. On her admission for TTP in 1996, her renal biopsy showed a thrombotic microangioma. Repeating renal biopsy would cause unnecessary morbidity in this case since the diagnosis is already quite certain.

Thrombocyopenia, often with purpura – This patient does have a significant thrombocytopenia, with a platelet count of 66. In addition large platelets and clumping of platelets were noted on the peripheral blood smear, but of which are indicative of TTP. Some purpura were noted on physical exam, but they were not particularly prominent.

Acute renal insufficiency that may be associated with anuria – This patient has acute renal failure, with a BUN of 119 and a creatinine of 13.6. She is oliguric (about 30 cc/hour), but not anuric.

Neurologic abnormalities, usually fluctuating – The patient has several notable neurological abnormalities, but several of these seem to be present at baseline for her. The two abnormalities that the patient and her daughter acknowledge are new are her significant daytime somnolence and her headaches. Headache is the most common neurologic symptom found in TTP.

Fever – The patient has been afebrile by history and has not had a fever in her first several hours in the hospital.

The presence of four out of these five diagnostic criteria is very suggestive for a diagnosis of TTP. In fact, "fever" is the most commonly absent of the diagnostic pentad for TTP, especially in newer case series. It has even been suggested that fever may not be a symptom of TTP at all, but may be caused by complications of TTP, such as sepsis.

Differential Diagnosis:

The main other diagnosis to consider in this clinical picture is diffuse intravascular coagulation (DIC). This diagnosis has been ruled out with a DIC screen that showed slightly elevated fibrinogen levels and undetectable levels of fragmented D-dimer. The presence of normal (or slightly above normal in this case) shows

that fibrinogen is not being consumed by DIC, and the absence of D-dimer also shows that the coagulation pathway is not actively taking place in this patient.

Precipitating Factors:

Most cases of TTP are idiopathic. In some cases, however, a single precipitating factor of TTP can found to be present. We will look for such a factor in this case, both to explain why the patient developed TTP and so that the precipitating factor can be treated. Potential precipitating factors include:

- Gastrointestinal infections, most commonly Shiga toxin-producing bacteria such as E. coli 0157:H7 – Fecal samples have been sent for fecal leukocytes, culture, fecal parasite screen, and C. dificil toxin.
- Drugs – The patient has not started any new drugs recently, and none of the drugs she is on are commonly known to precipitate TTP. Specifically, she does not take quinine or drink liquids high in quinine. Other drugs that are thought to precipitate TTP include cyclosporine, tacrolimus, OKT3, ticlopidine, clopidogrel, and valacyclovir. The patient is not on any of these agents.
- Antiphospholipid Antibodies – A screen for the antibody most commonly implicated antibody, anti-cardiolipin, has been sent and is pending. A screen for RBC IgG was negative
- HIV – HIV has been reported to precipitate TTP, so testing this patient for HIV will be considered.
- Cancer – Neoplastic processes can precipitate TTP, so once the patient is past the acute phase of her TTP, efforts will be made to improve her cancer screening, as well as her general health maintenance. Specifically, she should receive a colonoscopy, especially since she is guiac positive, and she should receive a mammogram since she has apparently not had one in several years.
- Pregnancy and Oral Contraceptives – The patient is not pregnant, nor does she take oral contraceptives or any other hormone therapy.
- Pneumococcal Infection – This patient does not have any signs or symptoms of pneumococcal infection.

Treatment

Treatment for TTP is plasmapheresis and administration of fresh frozen plasma (FFP). One randomized trial has shown this therapy to increase survival from 50% to 78% in patients with TTP (N Engl J Med 1991 Aug 8;325(6):393-7). A vascath has been placed in the patient's femoral vein, and she will receive plasmapheresis once a day, along with daily administration of FFP.

The rational behind this treatment is that plasmapheresis clears from the blood the anti-ADAMTS antibody, which causes ADAMTS13 deficiency and the resulting inability of the platelets to convert unusually large von Willebrand factor (ULVWf) to Von Willebrand factor (VWf). Transfusion of FFP helps to replete antibodies and other plasma proteins that are lost during the course of plasmapheresis. Anaphalaxic

and other anaphalactoid reactions occur commonly following transfusion of FFP, and are treated with epinephrine and corticosteroids when they occur.

If plasmapheresis is not showing a measurable result within several days, IV corticosteroid therapy will be added to this therapy. Approximately 10-15 percent of patients do not respond to plasmapheresis. These patients are thought to have ADAMTS13 deficiency due to some cause other than anti-ADAMTS13 antibody. Administration of corticosteroid is of questionable efficacy in these patients, but it is currently the only therapy available. Since this patient showed a very good response to plasmapheresis and FFP transfusion on her last admission, it is expected that she will show a positive response again.

2) Acute Renal Failure

This patient has acute renal failure, with a BUN of 119 and a creatinine of 13.6, on top of her preexisting chronic renal insufficiency (baseline creatinine is 1.7). The cause of this renal failure is TTP, so it will be treated by treating the underlying TTP, as described above. In addition, the patient's Lasix, Atenolol, and Norvasc are being held. These drug are being held both because they can impair renal function during episodes of acute renal failure, and because, in the setting of the large volume shifts associated with plasmaphoresis, they may complicate the clinical picture and make assessment of the patient's fluid status more difficult. Norvasc will be restarted if the patient becomes significantly hypertensive, and lasix can be administered if she develops pulmonary edema.

The patient currently has no indications for dialysis, but we will continue to monitor for these indications, such as acidemia, altered mental status, dangerous electrolyte abnormalities, volume overload, drug overdose, and symptomatic uremia. We will avoid giving patient any contrast dye as long as renal function is poor, and will take renal function into account when dosing medications. It is very posible that this patient's renal function will never return to it's baseline, and that she will suffer some permanent kidney damage as a result of this episode of TTP, just as she did during her last episode of TTP.

3) Anemia

This patient is anemic, with a hematocrit of 0.34. This is a hemolytic anemia, and is caused by her TTP. Treatment of this anemia will be to treat its underlying cause – TTP. She will be transfused if her hematocrit continues to fall or if she begins to show increased symptoms of anemia. The patient's type and screen will be kept up to date

4) Thrombocytopenia

This patient is thrombocytopenic, with a platelet count of 66. This is caused by her TTP, so its treatment will be to treat the TTP. She currently has no acute bleeds, is hemodynamically stable, and has no indications for platelet transfusion. The patient's Aspirin will be held during this hospitalization, because there is no need to inhibit the platelet function of a patient who is thrombocytopenic.

5) Diarrhea
The patient's diarrhea appears to be fairly mild, and it is not among her most significant complaints. It does not appear to be causing excessive volume loss or any electrolyte abnormalities. As described above, fecal samples have been sent for fecal leukocytes, culture, fecal parasite screen, and C. dificil toxin. If a treatable cause of her diarrhea is found, it will be treated appropriately.

6) Hypertenison
The patient's antihypertensives are currently being held to ensure adequate renal perfusion during her acute renal insufficiency. We will monitor the patient's blood pressure, and will reinstitue antihypertensive therapy if she becomes more than moderately hypertensive. This is especially important in this patient since she has a history of a hypertensive stroke.

7) Elevated transaminasaes
The patient has mildly elevated transaminases. Elevated transaminasaes are normally not associated with TTP, so this needs to be explained in some other way. A likely cause of these elevated levels is that the patient takes Lipitor. Her Lipitor will be held while she is in the hospital, because it may be complicating the clinical picture, and hypercholesterolemia is significantly less likely the cause morbidity or mortality while this patient is in the hospital than is her TTP.

8) Health maintenance
The details of this patient's health maintenance are currently unclear. Records will be obtained from her PCP. Once her TTP has been treated, follow up will be arranged with her PCP, and additional health screening will be encouraged. Specifically, she should receive a colonoscopy and a mammogram, as described above.

9) Prophylaxis
GI – Protonix, 40 mg PO daily
DVT – SVDs in place bilaterally. DVT is unlikely since the patient is thrombocytopenic.

10) Code status
This has been discussed with the patient and she desires to be a full code.

11) Disposition
The patient will need to stay in the hospital until this episode of TTP has resolved. We anticipate this will take approximately eight days, since her last episode of TTP resolved after eight days of therapy. TTP is however, a very serious disease with a significant mortality rate, so it is very possible that her TTP does not resolve quickly, or that other complications arise. It is also possible that her renal function will be significantly impaired after this hospitalization. Patient will most likely return to her home in Durham following discharge.

KF