



PGY- 2 case Presentation

Apoorv Deotare

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Outline

1. Review
2. Disease Pathogenesis
3. Differential Diagnosis
4. Diagnostic Criteria
5. Treatment
6. Patient Update

History of Present Illness

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- 42 y Nepali speaking Indian origin Male came to ER for
- ***New right-sided weakness – since 4 days***
- ***Increased left-sided stiffness – since about a week***
- ***Urinary retention – about a week***

ED Course

In the ED, patient's vitals were within normal limits aside from initial tachycardia (HR 113), which stabilized to 94 with IVF. He was given rectal aspirin and NS IVF bolus in the ED. Patient's labs were unremarkable aside from mild anion gap (14).

Medical History

Past Medical History

- **Right frontal stroke** (4/21) with **residual left-sided weakness**-MRI brain showed small right frontal ischemic stroke extending into right frontal cortex on convexity (subacute stroke) and also chronic appearing left head of caudate hemorrhage.
- DM type 2 - Diagnosed in 2019 — HBA1c - 6.9 %
- Hyperlipidemia
- HIV -1 /AIDS on Biktarvy since 7/8/2019 (last CD4 31-->110 on Bactrim and azithromycin)
- Depression – on Zoloft (Qtc 434)
- CMV -No retinopathy seen on exam OU, due for DFE 6/2020.

Past Surgical History

- Nothing Significant

Family History

- DM type 2 in Mother and Father

Social history

- Smoking – used to be . Quit smoking in 2011
- Alcohol – No
- Illicits - No
- Living situation – with wife and 2 daughters
- Occupation - Labor

Review of Systems

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Constitutional: Negative for appetite change, chills, fatigue, fever and unexpected weight change.

HENT: Negative for hearing loss, rhinorrhea, sinus pressure, sore throat and trouble swallowing.

Eyes: Negative for photophobia, pain and visual disturbance.

Respiratory: Negative for cough, choking, shortness of breath and wheezing.

Cardiovascular: Negative for chest pain, palpitations and leg swelling.

Gastrointestinal: Positive for **constipation (1-2 days)**. Negative for abdominal distention, abdominal pain, diarrhea and nausea.

Endocrine: Negative for polydipsia, polyphagia and polyuria.

Genitourinary: Positive for **difficulty urinating (Chronic but worsening for 1 week)**.

Negative for dysuria, flank pain, hematuria and urgency.

Musculoskeletal: Positive for **gait problem**. Negative for joint swelling, myalgias, neck pain and neck stiffness.

Skin: Negative for pallor and rash.

Neurological: Positive for **facial asymmetry (Chronic left facial droop)** and **weakness (Chronic left-sided and new right-sided weakness)**. Negative for light-headedness, numbness and headaches.

Psychiatric/Behavioral: Negative for agitation and confusion. The patient is not nervous/anxious.

Physical Exam

Physical exam

CVS /RS – NAD

Bowel sounds present but **hypoactive**

Muscle wasting left upper and lower extremities

Neurological: He was alert and oriented to person, place, and time. No sensory deficit. He exhibited

Abnormal muscle tone (*Increased stiffness of left upper and lower extremities*).

Left facial droop (chronic)

1/5 strength in left upper and lower extremities. Left upper extremity flexed at elbow and wrist and internally rotated shoulder with hand resting on chest

2/5 strength of right upper extremity with significant pronation and 3/5 strength of right lower extremity

Labs, Imaging, and Biopsies

Labs

Lab Results

Component	Value
WBC	3.8
Hemoglobin	13.8
Hematocrit	39.3 (L)
Platelets	120 (L)
MCV	91.4

Lab Results

Component	Value
Sodium	136
Potassium	3.8
Chloride	95 (L)
CO2	27
BUN	12
CREATININE	1.02
Glucose	154 (H)
Calcium	9.7

Lab Results

Component	Value
AST	37
ALT	44
Total Protein	8.3 (H)
Albumin, Serum	4.4
Total Bilirubin	1.3
Alkaline Phosphatase	77
INR	0.9
aPTT	25.0

Lab Results

Component	Value
Troponin I	<0.012

Sodium

8/2/2019 1743	136 *
8/3/2019 0037	137 *
8/4/2019 0553	132 * ▼
8/4/2019 1807	129 * ▼
8/5/2019 0010	128 * ▼
8/5/2019 1120	130 * ▼
8/5/2019 1757	130 * ▼
8/6/2019 0056	127 * ▼
8/6/2019 0647	129 * ▼
8/6/2019 1247	132 * ▼
8/7/2019 0157	131 * ▼
8/10/2019 1626	133 * ▼

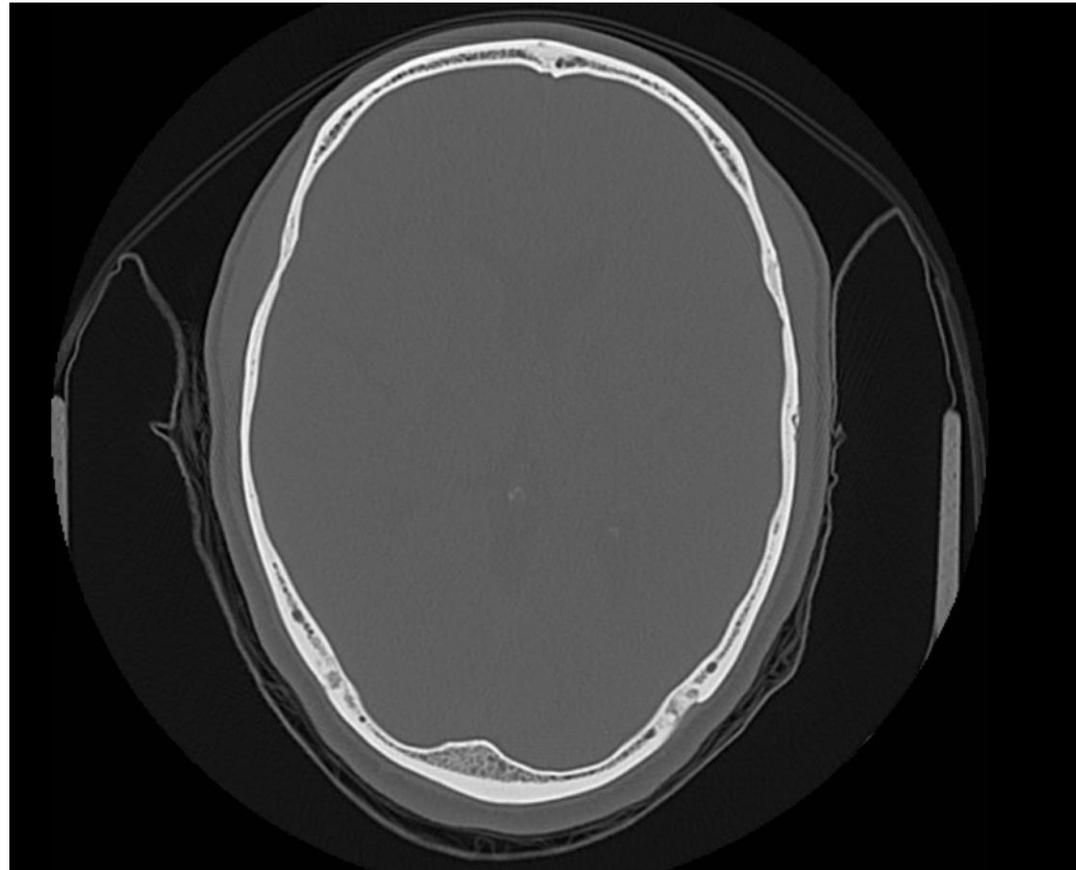
Serum Osmolality	Latest Ref Range: 280 - 300 mosm/kg	267 (L)
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Imaging

CT Head WO contrast –

-Old Right Frontal Infract unchanged

-**Hyperdensity** Lingering in the left caudate nucleus is probably calcification associated with the patient's previous hemorrhage



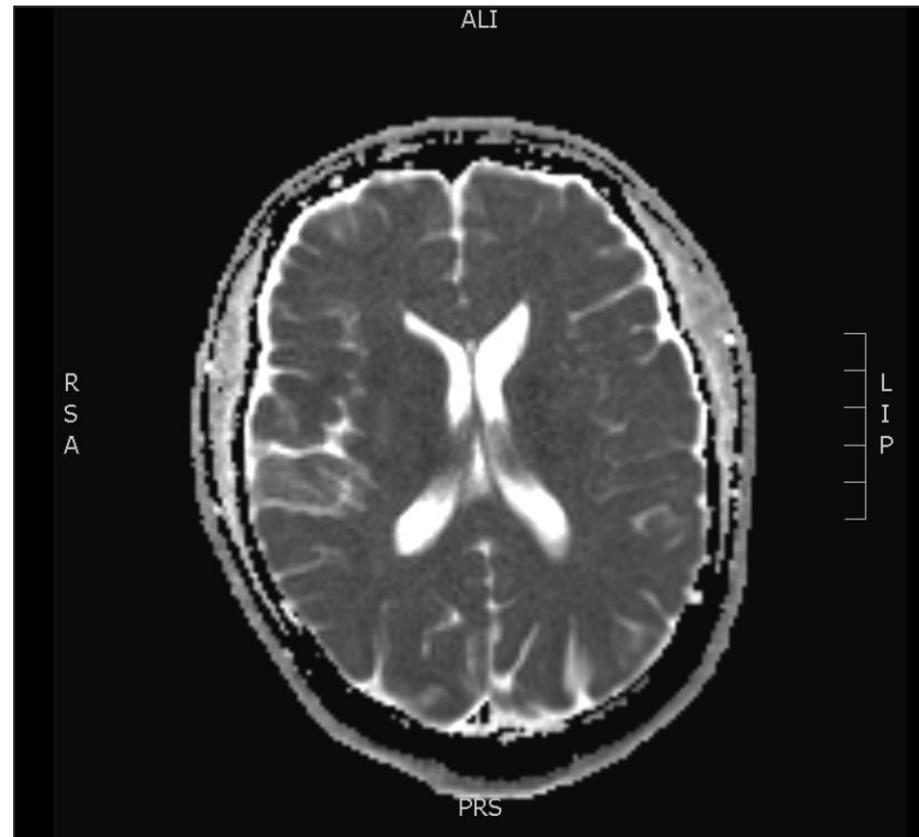
Course

- Neurology was on board – recommended to have **MRI studies** for more evaluation .
- As pt could not tolerate MRI multiple times, **LP was done** on on 8/5 and initial CSF results only notable for elevated oligoclonal bands, and an CSF JC Virus PCR was sent out to rule in PML
- Throughout his course, patient's **L sided weakness was stable yet unimproved**,
- Sodium dropped to 129 concerning for **SIADH vs Neurology Etiology** and therefore was put on fluid restriction as well and his Zoloft was stopped. Repeat sodium ranged in the low 130s yet the patient remained asymptomatic for discharge.
- Discharged to **SNF**

Imaging

MRI Brain W WO

- MRI Brain **limited 2/2 motion**, not consistent with stroke
- Restrictive Diffusion in right centrum semiovale** with evidence of **acute ischemia in Left centrum semiovale**
- Chronic white matter ischemic changes



CSF - Negative for Meningitis work up

Protein, CSF	73.7 ^	12.0 - 60.0 mg/dL
Myelin Basic Protein, CSF	9.75 ^	0.00 - 5.50 ng/mL
Oligoclonal Bands Number	5 ^	0 - 1 Bands
Oligo Bands	Positive !	NA

JC virus

Test Name	JC Virus
Result 1	see below
JC Virus Source:	CSF
JC Virus by PCR	DETECTED

Disease case is based on

Progressive Multifocal Leukoencephalopathy (PML)

- Severe demyelinating disease of the central nervous system that is caused by **reactivation** of the polyomavirus JC (JC virus)
- Remains **latent in kidneys and lymphoid organs**, but, in profound cellular immunosuppression, JC virus can reactivate, **spread to the brain, and induce a lytic infection of oligodendrocytes**, which are the CNS myelin-producing cells.
- Can occur in **AIDS (CD4 less than 200)** , Solid organ Transplant , lymphoproliferative and myeloproliferative diseases , SLE ,use of Immunomodulatory drugs like Natalizumab .
- Before widespread use ART , prevalence of PML in HIV was about 1% to 5 %
- Now , it occurs in about 1 to 3 cases per 1000 patients .
- PML has been rarely reported in HIV-infected patients in India and Africa. (lack of nonrecognition, lack of simple diagnostic tests, underreporting, premature deaths due to other infections)

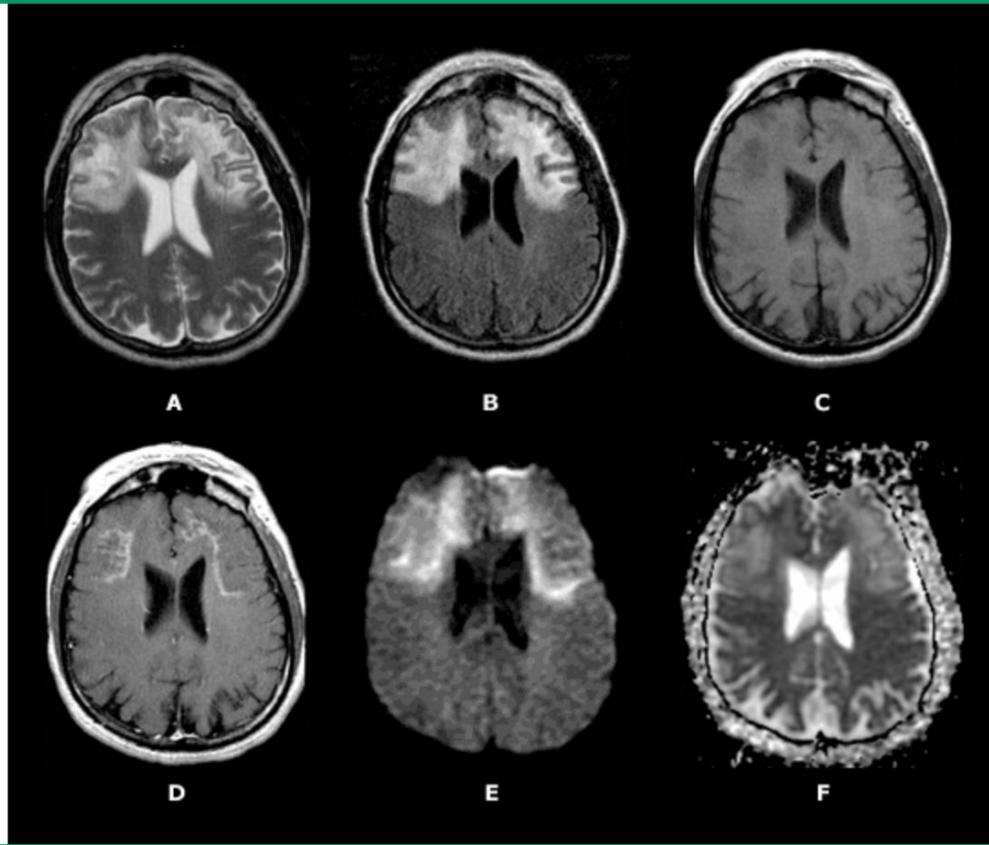
Clinical Manifestations

- **Classic PML** as name suggest – Progressive , multifocal, and involves the white matter.
- Subacute neurologic deficits including *altered mental status, motor deficits (hemiparesis or monoparesis), limb ataxia, gait ataxia, and visual symptoms such as hemianopia and diplopia.*
- *Can also cause cortical injury kind of picture – white matter lesions that undercut relevant cortical areas*
- *Aphasia , Cortical Blindness , Seizure*

*Survival is usually **FEW MONTHS***

MRI in PML

Brain MRI of progressive multifocal leukoencephalopathy after cardiac transplantation



Lesions of PML generally do NOT enhance with contrast or develop surrounding edema

Inflammatory PML

- New onset or clinical worsening of PML in patient getting ART
- Marked increase in CD4-positive T-cell counts and a decrease in HIV plasma viral load.
- Paradoxical development of PML is usually accompanied by an inflammatory reaction in PML lesions known as the **immune reconstitution inflammatory syndrome (IRIS)** and demonstrated by **contrast enhancement on brain MRI**.
- Co-occurrence of IRIS with PML has been observed also in patients with multiple sclerosis s/p Natalizumab.

- **JC virus can also cause**
 - JC virus cerebellar granule cell neuronopathy
 - JC virus encephalopathy
 - JC virus meningitis

Diagnosis

- Gold Standard – **Brain Biopsy**
 - sensitivity of 64 to 96 percent and a specificity of 100 %
 - triad of PML (demyelination, bizarre astrocytes, and enlarged oligodendroglial nuclei)
 - Risk of Morbidity / Mortality
- JC virus DNA in CSF - **PCR**
 - sensitivity of 72 to 92 percent and specificity of 92 to 100 %
 - ART-induced recovery of the immune system leads to decreased viral replication and clearance of JC virus DNA from CSF >>> ***False Negative***

Differential

- In HIV patients
 - HIV encephalopathy
 - primary central nervous system lymphoma (polymerase chain reaction for **Epstein-Barr virus +**)

PML –asymmetric, distributed throughout the white matter, well demarcated, and associated with focal neurologic deficits

HIV -symmetrical, poorly demarcated, and located in the periventricular areas , **not** with focal sensory, motor, or visual deficits.

Other D/D

- CNS vasculitis
- Reversible posterior leukoencephalopathy
- Varicella-zoster virus encephalopathy

Disease monitoring

- **JCV levels** may be prognostic markers in patients with PML.
- Low JCV burden (50 to 100 copies/mL) in the cerebrospinal fluid (CSF) had a longer survival than patients with high JCV burden
- **CD4-positive** T-cell counts **above 300** per mm³.
- Increased ratio of **myoinositol to creatine** . (Metabolite increases in brain inflammation)

Treatment

- Initiating or optimizing effective **antiretroviral therapy** (ART) for patients with HIV infection
 - ART – 50% survival for 1 year
 - Without ART – 10 %
- Withdrawing immunosuppressive drugs (when possible) for patients without HIV infection
 - cytarabine (2 mg/kg daily for five days) when the diagnosis of PML was established, and with mirtazapine.
- Discontinuing natalizumab and starting plasma exchange for patients with natalizumab-associated PML
- IRIS – Glucocorticoids if swelling >> brain Edema > herniation
 - intravenous dexamethasone (32 mg daily given in four divided doses) for two weeks, or intravenous methylprednisolone (1 g daily for five days), both followed by a slow glucocorticoid taper.

Pharmacological Treatment

- These drugs are **not** considered effective treatment for PML

Cytarabine - Decreases CV replication and multiplication in vitro

Nivalumab and Pembrolizimab

Topotecan

Mirtazapine

Maraviroc

Mefloquine

IL-7

Update on patient

- Re-admission
- ICU
- Medicine Floor

References

- UptoDate

Questions?

Thank you



Group B Streptococcus Endocarditis in Emerging Elderly Patient Population

Abhay Patel, PGY-2
Amy Billow, MS4
José Poblete, MD



Case Relevance

- To describe a rare but emerging case of Group B Strep (GBS) bacteremia and endocarditis in an elderly male with urinary complications
- To illustrate the difficulty in establishing a diagnosis of GBS endocarditis and the importance of pursuing a thorough workup in a patient with GBS bacteremia
- To emphasize the importance of familiarity with GBS endocarditis and further investigate its incidence



HPI

- 70 y/o M who presented with 5 days of fevers, myalgias, dysuria, hematuria, and bilateral flank pain
- ED Course: Sent by PCP. T100.9F, BP 91/51. CT abdomen/pelvis showed bilateral perinephric stranding and edema. Given 3L NS IVF boluses, ondansetron, 1x vancomycin, and piperacillin-tazobactam. Admitted for sepsis 2/2 acute pyelonephritis.



Other Medical History

Past Medical History: COPD, OSA, BPH, HTN, HLD, prediabetes, GERD, afib s/p ablation in 2016 (not on OAC), nephrolithiasis

Past Surgical History: Ablation (2016), removal of ingrown toenail (2018)

Allergies: None

Home Medications: Albuterol, Umeclidinium-vilanterol (LAMA, LABA), CPAP, tadalafil, rosuvastatin, esomeprazole

Social Hx: No EtOH for 31 years, former smoker (55 pack years, quit in 2006), no illicit substances or needle exposure. Occupation: manual labor at warehouse



Physical Exam

Vitals: temp 101.9F, RR 20, HR 101, BP 91/51, satting 97% on room air

General: Alert. Lying supine with head of bed elevated, in no acute distress

HEENT: Atraumatic, normocephalic. PERRLA, EOM intact. Moist mucous membranes. No visible polyps. No oral ulcers or other lesions

Heart: **Tachycardia, initially regular rhythm**, no m/r/g, normal S1 and S2, peripheral pulses intact/symmetric

Lung: Scattered expiratory wheezing, no use of accessory muscles for respiration

Abdomen: **Mild tenderness to palpation of flanks**, no guarding or rebound, no ecchymoses, normal bowel sounds

Extremities: No pedal edema, erythema, tenderness, deformity

Skin: **Janeway lesions appearing later in hospital course**

Psychiatric: Normal affect

Figures 1 and 2: Janeway Lesions





Labs

Table 1: Pertinent Labs with Results

Lab	Result
BMP	BUN 56 / Cr 3.66 (Baseline Cr 1.0)
CBC	WBC 7.4, ANC 6.4
Procalcitonin	9.76
Urinalysis	Turbid, moderate bacteria, 11-25 WBCs, negative nitrites
Liver Function Tests	AST 72, ALT 65
Hepatitis C Antibody	Negative

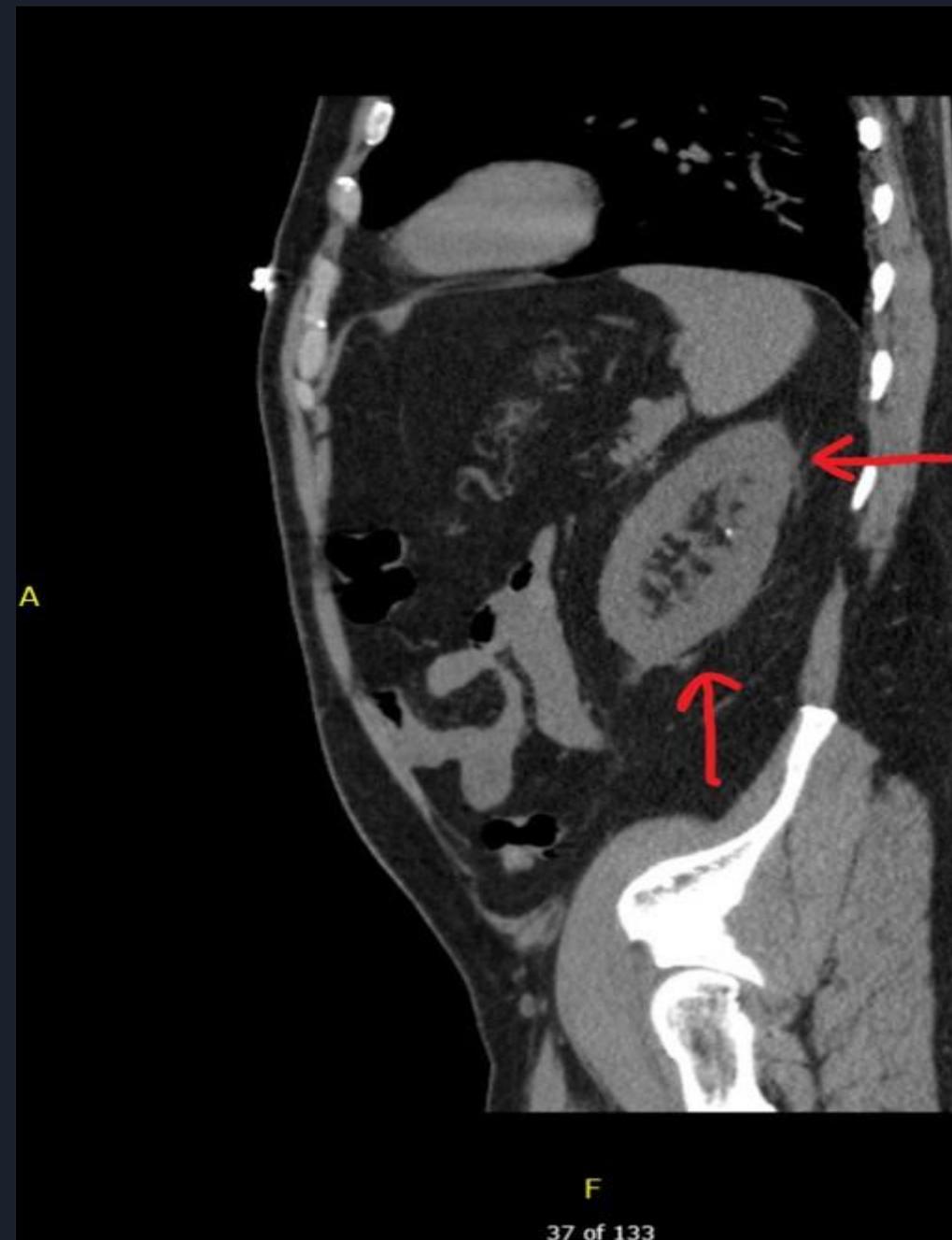
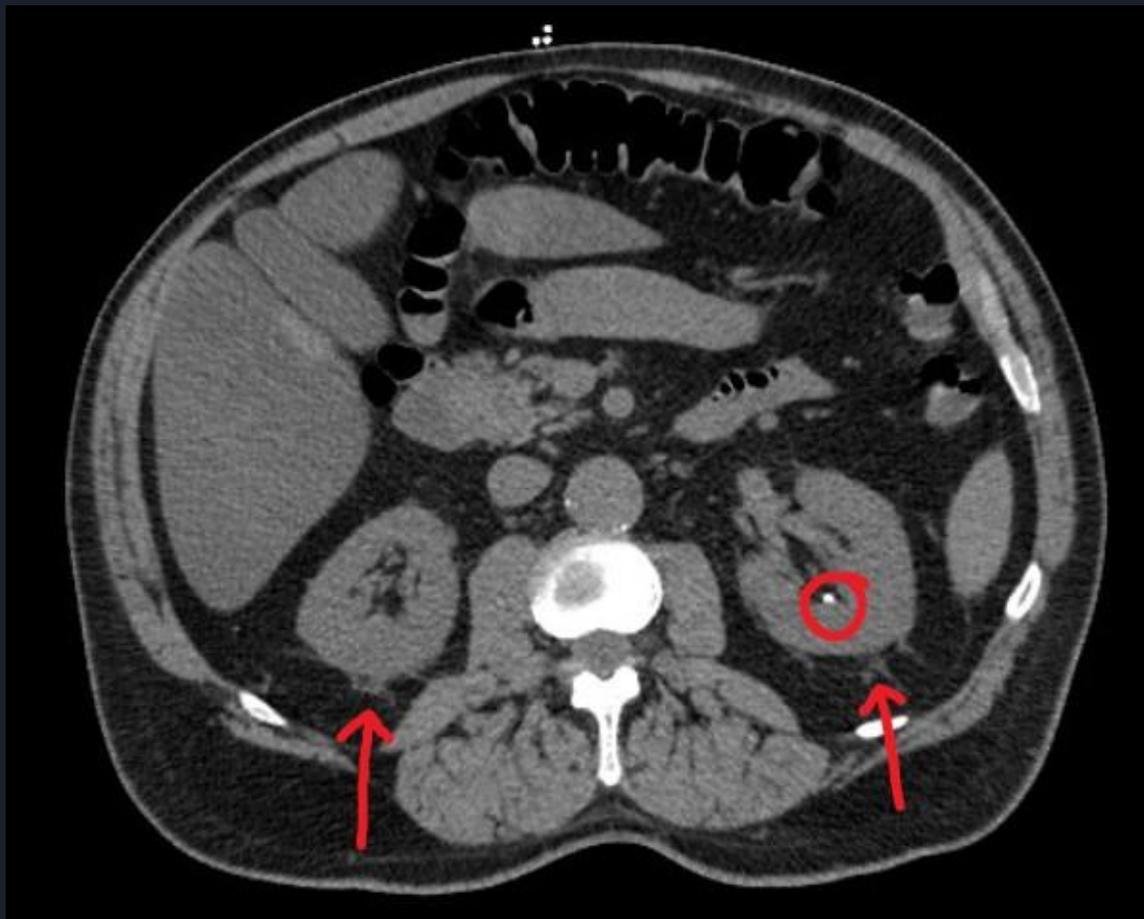


Initial Imaging

Table 2: Initial Imaging Studies with Results

Imaging Study	Result
CT abdomen/pelvis w/o contrast	Nonobstructive left renal calculus, bilateral perinephric stranding and edema . Also showed small hiatal hernia, colonic diverticulosis, bilateral fatty inguinal hernias
Retroperitoneal Ultrasound	No acute process. Fatty liver
TTE (Day 4)	EF 63%, grade II diastolic dysfunction, moderately dilated left atrium, mildly thickened leaflets of mitral valve

Figures 3 and 4:
Perinephric Stranding and
Nonobstructive Renal Calculus





Pathology

Table 3: Cultures with Results

Culture	Result
Urine Culture (Obtained Day 1)	No growth
Blood Cultures x2 (Obtained day 1)	Strep agalactiae (GBS)
Repeat Blood Cultures x2 (Obtained Day 4)	No growth



Initial Hospital Course

- Day 1: Initiated on IVF and pip-tazo. Fever resolved
- Day 2: Retroperitoneal ultrasound showed no acute findings
- Day 3: Blood cultures resulted in GBS. ID consulted. Patient switched from pip-tazo to cefazolin
- Day 4: TTE negative for vegetations. Repeat blood cultures obtained. Patient went into a fib w/ RVR. Received metoprolol PO and IV, but remained in a fib
- Day 5: EP consulted. Administered furosemide, maintained metoprolol PO, started Eliquis. TEE was performed in joint decision between teams



Imaging Cont'd

- TEE (Day 6): EF 55%. 1.2 cm (L) x 1.1 cm (W) vegetation on the atrial aspect of the anterior leaflet consistent with infective endocarditis. Small 0.5 cm (L) x 0.5 cm (W) mobile vegetation on the atrial aspect of the tip of the posterior leaflet. Mild 1+ regurgitation directed centrally



Final Hospital Course

Day 6: Janeway lesions now visible. EP initiated amiodarone for rhythm control of a fib. Converted to NSR. ID switched antibiotics to IV ampicillin

Day 7: Received PICC line. Planned for 4 weeks IV ampicillin

Day 8: Patient is discharged to home with plans for private outpatient IV infusions



Discussion

- GBS Bacteremia and endocarditis, though still rare, is becoming more common in elderly population.¹
- Endocarditis occurs in roughly 1.7% of GBS bacteremia and nearly all cases are in patients with history of diabetes, alcohol abuse, cirrhosis, or cancer.² Our patient did not meet any of these risk factors.
- GBS portends a high mortality, suggesting more virulence than other strep species. **However, in the absence of peripheral vascular or immunological stigmata, cardiac murmur, risk factors, and with a resolving fever, diagnosis of GBS infectious endocarditis may be difficult.**
- Let's illustrate this with our patient...

Table 4: Modified Duke Criteria

Major Criteria	2 separate positive blood cultures for microorganisms typical for infective endocarditis (strep viridans, bovis, HACEK, staph aureus, enterococci)
	Endocardial involvement on echocardiogram (valvular lesions, vegetation, abscess, partial dehiscence of prosthetic valve)
Minor Criteria	Predisposing heart condition or IVDA
	Temperature >38C (100.4F)
	Vascular phenomena (emboli



Discussion Continued

- In our patient, Janeway lesions did not show up until later in hospital course (after TEE performed). No murmurs or other physical exam findings to suggest endocarditis until a fib 4 days into hospital course
- Important to remain **astute** when we obtain positive GBS blood cultures and to remain **thorough** in our workup. This will help guide clinicians to the most appropriate treatment course and duration in this disease process with a high mortality rate
- Case also illustrates the need to further investigate the **incidence** of GBS endocarditis and its **potential complications**



Literature Cited

1. Francois Watkins LK, Mcgee L, Schrag SJ, et al. Epidemiology of Invasive Group B Streptococcal Infections Among Nonpregnant Adults in the United States, 2008-2016. *JAMA Intern Med.* 2019;179(4):479-488.
2. Teran CG, Antezana AO, Salvani J, Abaitey D. Group B streptococcus endocarditis associated with multiple pulmonary septic emboli. *Clin Pract.* 2011;1(1):e7.
3. Li JS, Sexton DJ, Mick N, et al. *Clinical Infectious Disease* 2000; 30:633