A Transplant Recipient with Asterixis

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Background

- Hyperammonemia Syndrome of Transplant (HS) is a rare clinical entity occurring post-transplant, best described after lung transplant (LT).
- Characterized by overwhelming ammonia levels, cerebral edema and fatal if untreated.
- Specific cause of HS not known until 2015[1]

HPI

A 71 year old male with a history of IPF admitted electively for LT

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Underwent LT, extubated on postoperative day (POD) 2

Treated with ceftriaxone given donor sputum culture positivity for *H. Influenzae.*

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POD 10 - On ceftriaxone, developed a swelling at clamshell thoracotomy wound, underwent I&D.

Gram stain and routine cultures negative- presumed seroma.

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POD 18 - required repeat I&D despite ongoing ceftriaxone .

Switched to combination Vancomycin and Piperacillin-Tazobactam repeat cultures obtained.

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POD 20 - Routine chest x-ray demonstrated a left-sided pleural effusion.

Aspirated and a chest tube was placed.

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POD 23- Pleural fluid culture and wound swab grew candida, the patient was started on micafungin.

Asymptomatic and working with PT through this time.

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POD 24 progressive encephalopathy leading to obtundation and disorientation

History, Exam and Labs

Past History:

- IPF, requiring 10-15 LPM of oxygen pre-transplant, was on MMF (mycophenolate mofetil) pre transplant
- No relevant travel, family or exposure history
- LT-related data:
  - Serology: CMV D+/R+, EBV R+, VZV R+, HSV 1/2,R - Both D&R were negative for Hep B s Ag, Hep B c Ab, Hep C Ab.
  - Donor sputum positive for pan susceptible *H. Influenzae*.

Medications per LT protocol:

- Basiliximab and steroids for induction
- Tacrolimus, MMF, tapering steroids for maintenance
- Valganciclovir for CMV/HSV and Bactrim for PJP prophylaxis

Therapeutic antibiotics:

- Ceftriaxone days 0-16
- Vancomycin and Piperacillin/Tazobactam days 18-24
- Micafungin 100mg q24h day 23-24

Pertinent physical examination findings at the time of encephalopathy

HR 112/min, BP 115/85, T 98 °F, RR 18/min SpO2 96% on 2 L.

- Drowsy, responds to voice. Able to follow basic commands only
- PERRLA, EOMI, no Nystagmus, no facial asymmetry
- He appreciates sensation and is able to move all 4 limbs.
- Marked asterixis.
- Dehisced clamshell thoracotomy wound with wound vacuum in place, only trace redness at margins.

Laboratory and radiologic data available at time of evaluation

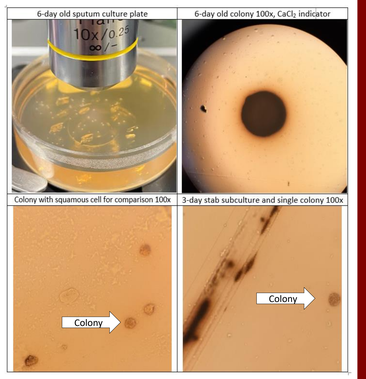
- WBC 11.5k/mm^3- 85% neutrophils
- Creatinine 0.99 mg/dl, BUN 42 mg/dL
- CRP 110 mg/L
- Unremarkable Electrolytes and liver enzymes.
- Tacrolimus level 10.1 ug/L (at target)
- CT head was normal
- Pleural fluid: 1k Nuc cells, 45% Neut, 41% Mono, 15% Lymph, Prot 2.5 g/dL, Gluc 102 mg/DL, LDH 1174 U/L
- Pleural fluid culture: *C. albicans*
- Wound swab *C. dublinensis*
- Blood culture: No growth

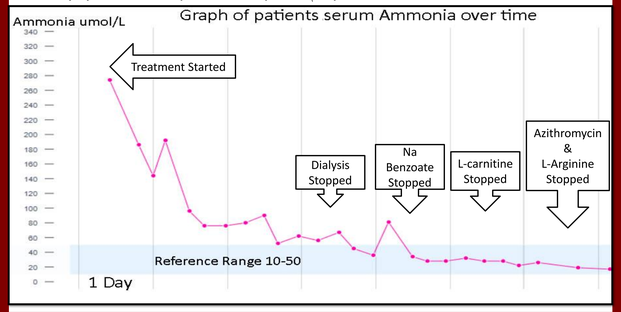
Differential

1. Reactivation viral encephalitis [CMV, VZV]
2. Donor derived viral encephalitis [HSV, WNV]
3. Opportunistic infection: Cryptococcus, toxoplasma
4. Septic encephalopathy secondary to fungemia
5. Urease producing organism infection
6. Hepatic Encephalopathy/Acute Liver Failure
7. Toxic effect of medication / calcineurin inhibitor toxicity.

Hospital Course

- Ammonia level: **274 umol/L** [ref 10-50]
- Respiratory, wound and pleural fluid culture: Positive for ***Ureaplasma urealyticum*** by PCR and culture, pleural culture positive for *Mycoplasma hominis*
- Urine *Ureaplasma* PCR negative, culture positive for *Mycoplasma hominis*
- Started on **Doxycycline 100 mg BID + Azithromycin 500 mg qD.**
- Additionally treated with hemodialysis, L-arginine, levocarnitine and sodium benzoate.
- Mental status improved within 24 hours, repeat pleural fluid cultures negative on day 5.
- Completed a 7-day course of azithromycin and continued doxycycline until post-transplant day 100.





Final Diagnosis

Disseminated *Ureaplasma urealyticum* infection following lung transplantation leading to hyperammonemia syndrome

Hyperammonemia Syndrome

- HS of transplant is caused by excessive production of ammonia by urease producing organisms[2].
- Typically occurs in first 7-14 days post transplant.
- *Ureaplasma* is a species of the order mollicutes and is notable for the absence of a cell wall and the production of ammonia. The lack of a cell wall leads to lack of positivity on gram stain, and difficulties with culture.
- *Ureaplasma* grows in nutritionally enriched media in the lab with characteristic small colonies, and preferential growth in stab culture.
- Antimicrobial resistance is a growing problem in Ureaplasma[3].
- In a series[4] 28% of post-LT patients were positive for *Ureaplasma* species, however only 2% developed disease
- Donor characteristics (younger age, female sex and high-risk sexual behaviors)[5]have been associated with higher rates of post-transplant *Ureaplasma* PCR positivity.
- Mortality remains high with rates of between 25-38% in available case series.
- We hypothesize that our case may have been donor derived but were unable to confirm this.

Conclusions

- We present a case of disseminated *U. urealyticum* infection involving a wound and respiratory organs leading to HS.
- A high index of suspicion is needed in cases of encephalopathy post organ transplant.
- In severe cases aggressive multimodal therapy is essential due to high mortality.
- Further study is required to determine optimal screening, prophylaxis and treatment

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