



MYCOTIC KNEE INFECTION IN AN INFANT

Taking a closer look at *Candida* arthritis
and diagnostic markers in septic arthritis

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Disclosure

- I have no actual or potential conflict of interest in relation to this presentation
- I have no financial relationships to disclose



The Case

DR is a 5mo infant with complicated PMH including TOF + long NICU stay presenting to office with refusal to move her left leg

- No redness or warmth
- No swelling
- No fevers
- No change in activity
- Recent cath

□ PMH

- Term VSD 22yo G2P1, no preg complications
- TOF with Pulmonary Atresia
- NICU (4 months)
 - Central Shunt, PDA Ligation at 2 weeks
 - Complete Repair at 3.5 months
 - Prolonged ventilation, thrombosis of LFV-infrahepatic IVC, central line infection with Candidemia
- Cath: Bilat fem vv occlusion, no visualized subhepatic IVC



The Case

□ Medications

- Aspirin 40.5mg qd
- Ranitidine 20mg BID

□ Vital Signs

- HR: 151
- R: 40
- T: 36.9 °C
- BP: 99/54

□ Physical Exam - Pert

- NAD, well-nourished
- RRR, II/VI sys M + Soft early dia M, 2+ pulses, Cap refill <3 seconds
- R leg normal
- L knee difficult to straighten, crying with manipulation. L hip + foot normal. No erythema, no swelling.
- L groin cath site well healed

The Case

□ Labs

WBC	12
Hb	10.8
Plt	640
Gran	51%
Lym	31%
Mon	13%

ESR	76
CRP	82

WBC knee	70,047/ mm³
Gran	91%
Lym	8%

□ Imaging

- **Ultrasound:** Left hip unremarkable. Right hip unremarkable. Right knee unremarkable. Left knee complex suprapatellar joint effusion measuring 3.0 x 0.7 x 2.5 cm.

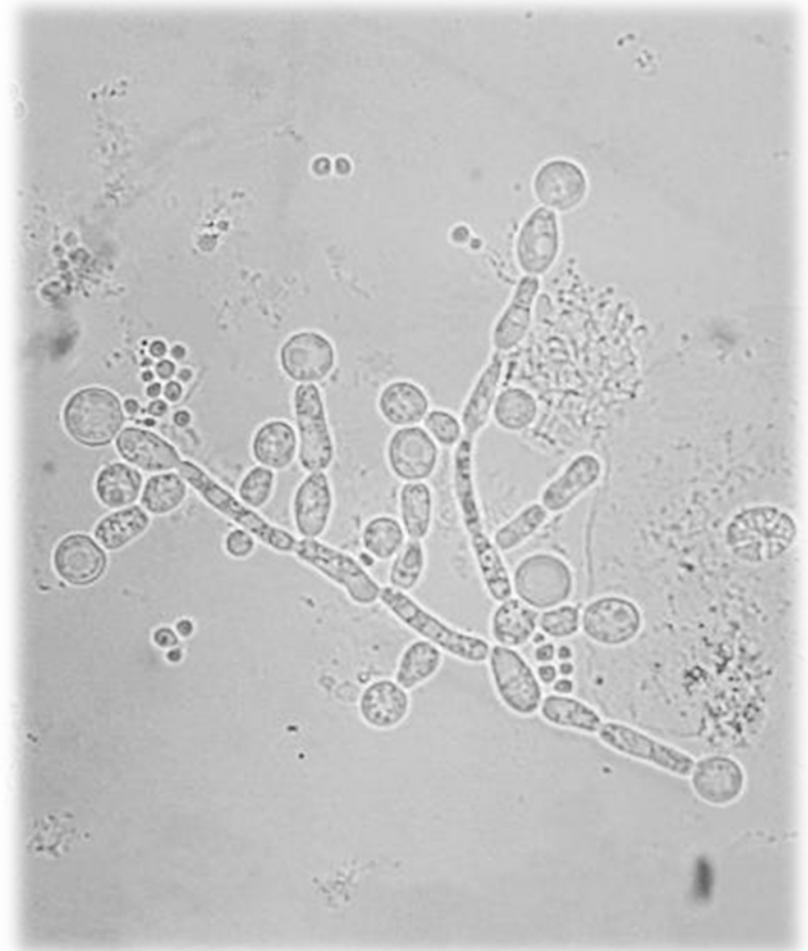


Hospital Course

- **Day 1:** Ceftriaxone + Vancomycin initially, with Linezolid and Cefdinir for a period of time when IV access was lost
- **Day 4:** Culture grew *Candida albicans*, discontinued antibiotics and started IV fluconazole
- **Day 7:** CRP continued to rise (144.1), fluconazole dc'd, started micafungin, restarted linezolid + ceftriaxone; repeat aspiration of knee (again grew *Candida albicans*)
- **Day 7-13:** Downtrend of CRP to 56.1
- **Day 13:** Discontinued linezolid + ceftriaxone; Micafungin continued for full 14 day course
- **Day 15:** CRP 8.7
- **Day 16:** Repeat aspiration of joint fluid – negative for any growth
- **Day 18:** Discharged home

Candidal Septic Arthritis

- 63% h/o candidemia
- Hematogenous (81%, children 90%) vs direct inoculation (19%)
- Usually monoarticular
- Knee > Hip > Shoulder
- 63% *Candida albicans*
- Only 13% had fever
- Among children, 70% were neonates or infants



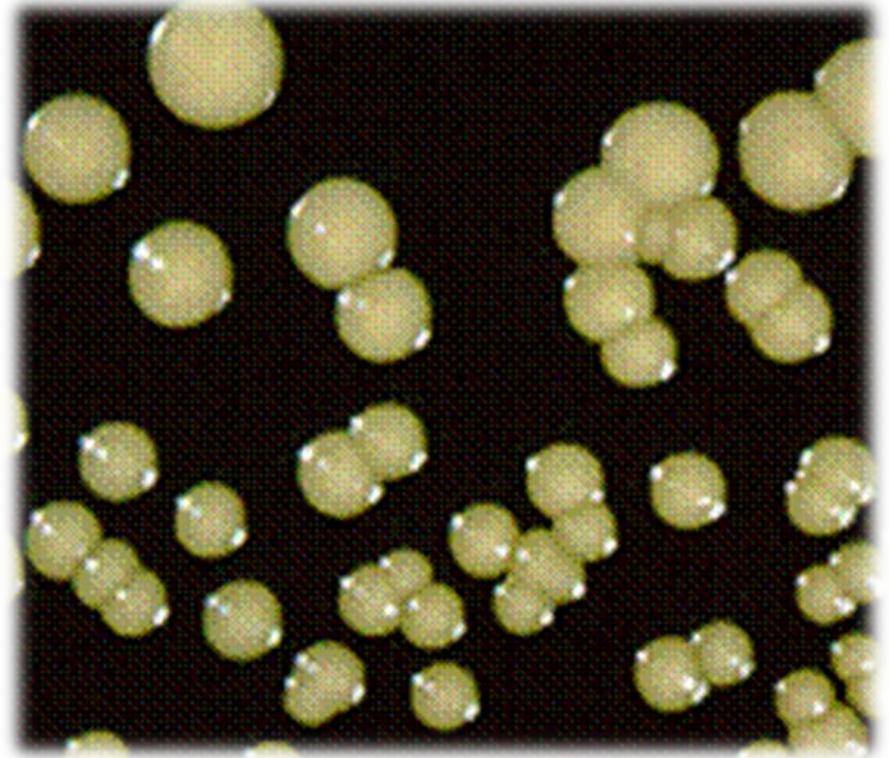


IDSA Candida Guidelines

- 1. Fluconazole daily for 6 weeks OR echinocandin for 2 weeks followed by fluconazole for at least 4 weeks
- 2. Lipid formulation AmB followed by fluconazole is a less desirable, but acceptable alternative
- 3. Surgical drainage is indicated in all cases of septic arthritis

When to consider Candida?

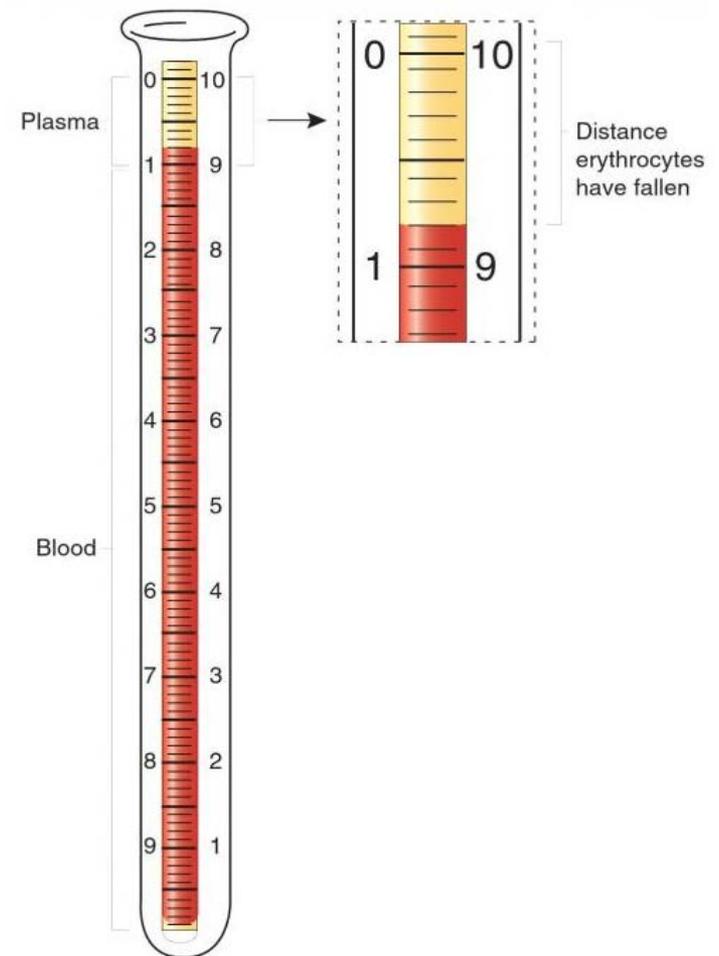
- History of Candidemia
- Patient with underlying immunosuppression, or recent neutropenia
- Presence of central venous catheters
- Lack of favorable response to treatment with antibiotics



<http://www.life-worldwide.org/fungal-diseases/candida-albicans>

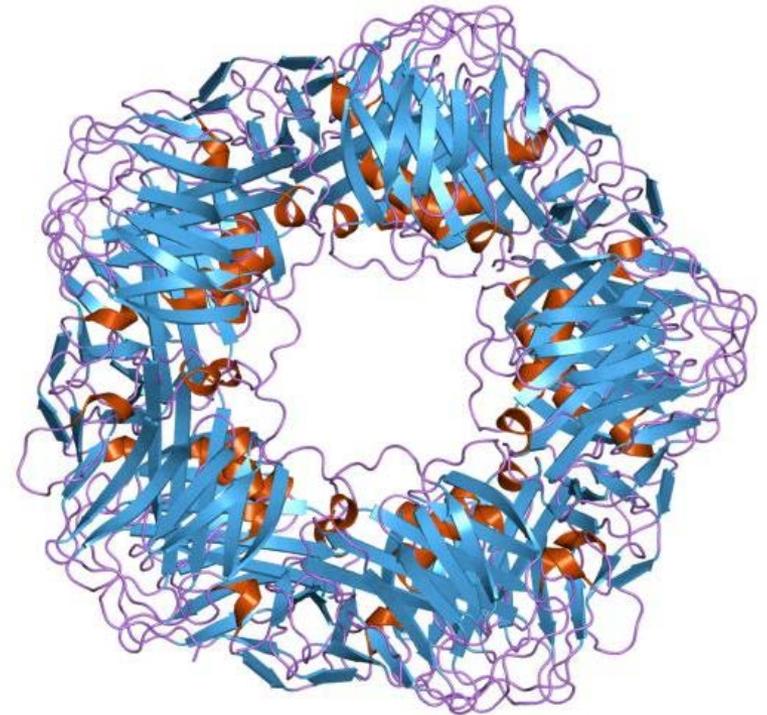
ESR – Erythrocyte Sedimentation Rate

- Rate of fall of erythrocytes, mm/hr
- Inflammation = lower electrostatic charge on RBC surface
- Part of Kocher criteria
- Better for diagnosis than for trending
- Moderately elevated in Candidal septic arthritis



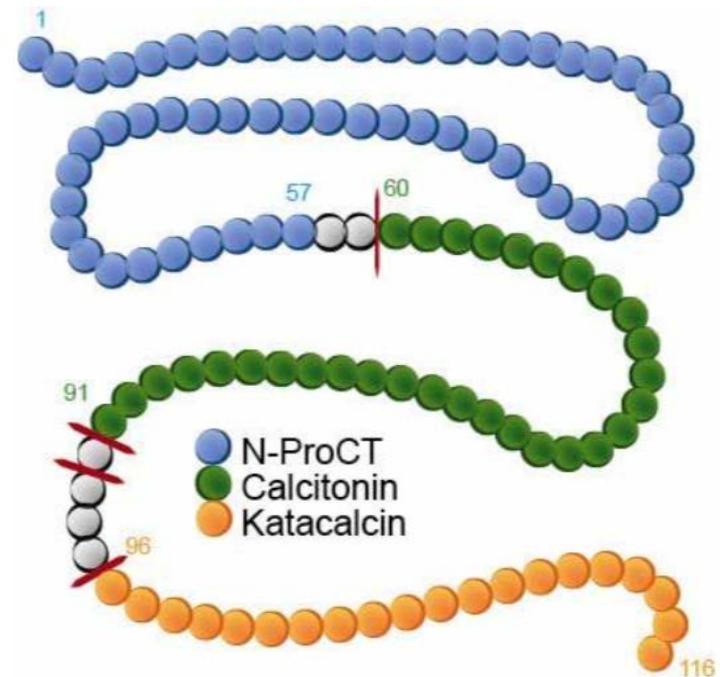
CRP – C-Reactive Protein

- Binds to “C” polysaccharide
- Synthesized by hepatocytes
- Peaks 2-3 days, half-life 19 hours
- Marked increase $>10\text{mg/dL}$, most studies $>20\text{mg/dL}$
- Use to ensure adequacy of therapy, and transition to oral therapy



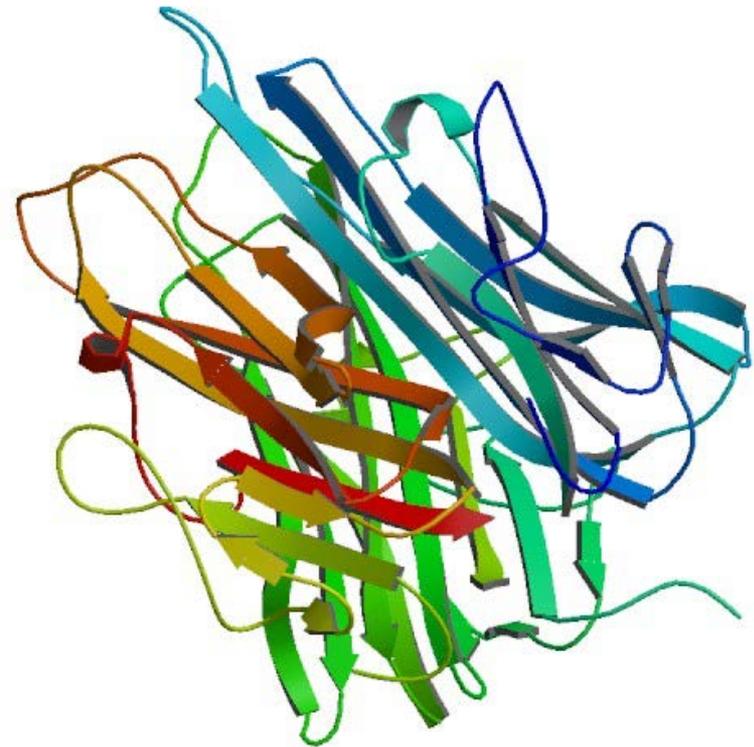
Procalcitonin

- Detectable within 4 hours, half-life 22 to 29 hours
- In general, only increases in presence of bacterial infections
- Fungal infections?
Arthritis?
- Significant potential as a biomarker



Novel Inflammatory Markers

- Leukocyte esterase via urine dipstick
- PCT in synovial fluid
- TNF- α
- IL-6
- CD-64



TNF- α

<http://www.rcsb.org/pdb/explore/explore.do?structureId=1TNF>



CONCLUSIONS

- Baby DR fully recovered
- Likely an exciting future for biomarkers
- New IDSA guidelines Spring 2017

Citations

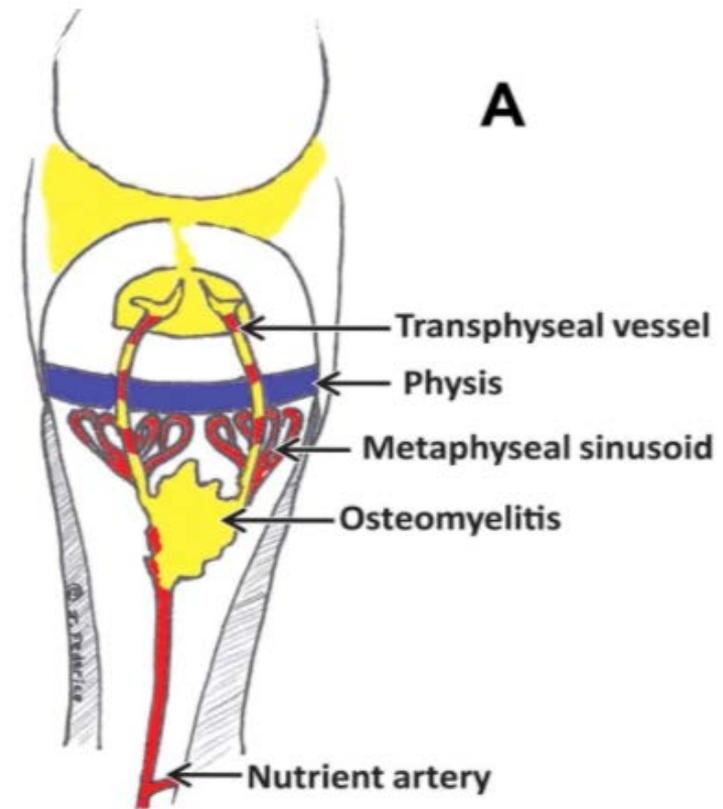
- Arnold, John C., et al. "Acute bacterial osteoarticular infections: eight-year analysis of C-reactive protein for oral step-down therapy." *Pediatrics* (2012): peds-2012.
- Arnold, John C., and John S. Bradley. "Osteoarticular infections in children." *Infectious disease clinics of North America* 29.3 (2015): 557-574.
- Colvin, Otis C., et al. "Leukocyte esterase analysis in the diagnosis of joint infection: Can we make a diagnosis using a simple urine dipstick?." *Skeletal radiology* 44.5 (2015): 673-677.
- James D. Cherry, Gail J. Harrison, Sheldon L. Kaplan, William J. Steinbach, Peter Hotez. Feigin and Cherry's Textbook of Pediatric Infectious Diseases. Philadelphia, PA :Elsevier/Saunders, 2014. Print.
- Dornbusch, H. J., et al. "Procalcitonin—a marker of invasive fungal infection?." *Supportive care in cancer* 13.5 (2005): 343-346.
- Gamaletsou, Maria N., et al. "Candida Arthritis: Analysis of 112 Pediatric and Adult Cases." *Open forum infectious diseases*. Vol. 3. No. 1. Oxford University Press, 2016.
- Gutierrez, Kathleen. "Bone and joint infections in children." *Pediatric clinics of North America* 52.3 (2005): 779-794.
- Hugle, T., et al. "Serum procalcitonin for discrimination between septic and non-septic arthritis." *Clinical & Experimental Rheumatology* 26.3 (2008): 453.
- Kushner, I., and S. P. Ballou. "Acute-phase reactants and the concept of inflammation." *Firestein G, RC RB, Harris E, al e. editors. Kelley's Textbook of Rheumatology* 8 (2008).

Citations Cont.

- Lenski, Markus, and Michael A. Scherer. "Diagnostic potential of inflammatory markers in septic arthritis and periprosthetic joint infections: a clinical study with 719 patients." *Infectious Diseases* 47.6 (2015): 399-409.
- Long, Sarah S., Larry K. Pickering, and Charles G. Prober. *Principles and practice of pediatric infectious disease*. Elsevier Health Sciences, 2012.
- Luhmann, Scott J., et al. "Differentiation between septic arthritis and transient synovitis of the hip in children with clinical prediction algorithms." *The Journal of Bone & Joint Surgery* 86.5 (2004): 956-962.
- Maharajan, Karthikeyan, et al. "Serum Procalcitonin is a sensitive and specific marker in the diagnosis of septic arthritis and acute osteomyelitis." *Journal of orthopaedic surgery and research* 8.1 (2013): 1.
- Oppegaard, Oddvar, et al. "CD64 as a potential biomarker in septic arthritis." *BMC infectious diseases* 13.1 (2013): 1.
- Pääkkönen, Markus, et al. "Sensitivity of erythrocyte sedimentation rate and C-reactive protein in childhood bone and joint infections." *Clinical Orthopaedics and Related Research*® 468.3 (2010): 861-866.
- Pappas, Peter G., et al. "Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America." *Clinical Infectious Diseases* (2015): civ933.
- Talebi-Taher, Mahshid, et al. "Septic versus inflammatory arthritis: discriminating the ability of serum inflammatory markers." *Rheumatology international* 33.2 (2013): 319-324.
- Wagner, Scott, and Jefferson Jex. "Delayed *Candida albicans* Septic Arthritis in a Pediatric Patient with Cerebral Palsy." *JBJS Case Connector* 4.3 (2014): e70.

Neonates and Infants

- <18moa Transphyseal vessels – increased risk of mixed septic arthritis + osteomyelitis
- Reduced rate of blood flow – more susceptible to seeding
- Thinner periosteum





ESR and CRP

- Both very sensitive, especially when used together
- ESR = Diagnosis
- CRP = Diagnosis + Trending during treatment
- Neither is very specific
- Negative predictor > Positive predictor
- Candidal arthritis: Both are moderately elevated