

# Community-acquired MRSA Septic Thrombosis in Previously Healthy Children - 2 Case Reports

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## Goals for Talk

- Case presentations
- History of MRSA
- Virulence factors
- Differences between community-acquired (CA-MRSA) and healthcare-associated MRSA (HA-MRSA)
- Incidence and epidemiology of MRSA
  - Nationally
  - Locally

## Case 1- History

- Almost 5 year old previously healthy boy with
  - 2 day history of LLE pain
    - Knee pain not relieved by Tylenol
    - Intermittent tactile fever
    - Seen by PMD -
      - afebrile, no relief from ibuprofen and Tylenol
      - BC, CBC, ESR sent
  - 1 d PTA
    - Pain "walked up leg to hip", burning
    - Walked with limp
    - Unable to sleep due to pain
  - DOA
    - Would not bear weight on leg
    - c/o lower back and hip pain
    - Mother noticed onset of slight thigh edema
  - Good po intake until doa
  - No significant PMH or PSH

## Case 1 - Presenting PE

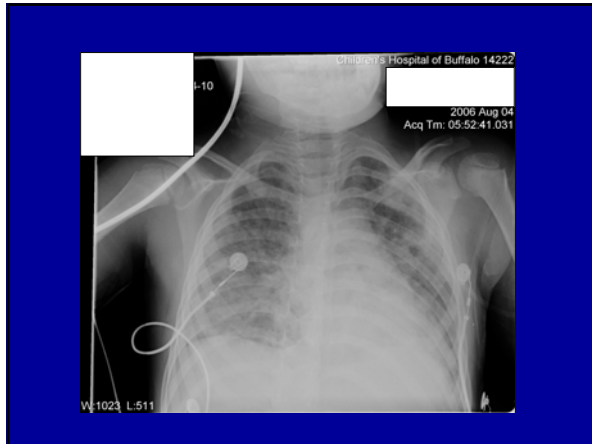
- In ED: (15:30)
  - T=36.1 °C HR = 170 RR = 28 BP = 99/64 wt = 22.5 kg
  - Sleepy, pale
  - Tachycardic
  - Clear lungs
  - L knee @45 °, very tender to movement, no effusion, edema, erythema
  - Bilateral hip pain

## Case 1- Course HD1

- On floor (23:00)
  - T=36.1 °C HR = 175 RR = 28 BP = 99/41
  - Uncomfortable, frog-legged position
  - Fine papular rash on chest
  - Tachycardic, normal pulses
  - Abd: mild distension, diffusely tender
  - L thigh = 37cm, R thigh = 35 cm, pain with L hip flexion, extension, rotation, point tenderness L hip, no erythema, no knee effusions or pain, no calf tenderness
- Outpatient studies
  - WBC = 12.7 with 59% segs, 33% bands
  - ESR = 39
  - knee x-ray normal
  - Rapid strep +
- Treatment
  - Amoxicillin
  - Pain meds - Morphine, Tylenol, ibuprofen

## Case 1- Course HD2

- 04:45
  - Afebrile
  - Tachycardic (HR = 170's), BP = 90's/50's
    - 20 ml/kg IVF HR = 150, BP = 108/45
    - EKG - sinus rhythm
  - Grunting respirations with RA sats 93%
  - Abd distension
  - Grossly edematous L thigh with erythema extending to lower abd
  - Posterior thigh and calf tenderness
  - Petechiae on L thigh
  - Pustules on abd, R axilla
- PICU consult
- Ultrasound of LLE ordered



## Case 1- PICU Course HD2

- 05:15
  - T=37.7°C HR=176 RR = 38 BP = 80/40
  - Crying in pain
  - Lungs: ↓ aeration at bases
  - Tachycardic, cap refill < 3sec
  - Pustules & erythema on abd
  - L thigh swelling with erythema extending to buttock and knee

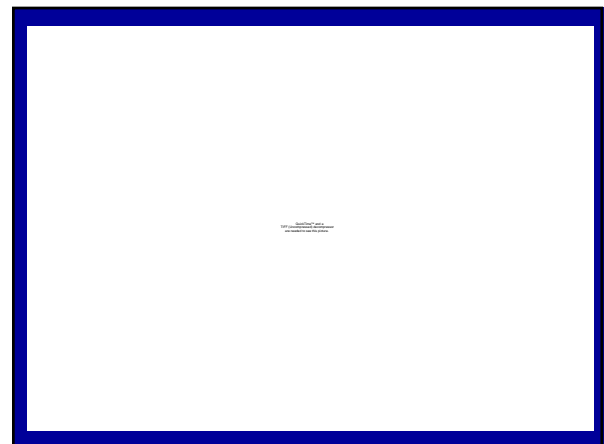
## Case 1- PICU Course HD2

- Labs:
  - WBC = 2.3 with 16% segs, 72% bands, toxic granulations
  - Na+ = 132
  - Lactate = 2
  - VBG = 7.30/44/-5
  - PT = 20.4 PTT = 43.9 INR = 1.75 Fibrinogen = 541 FSP>20
- Studies:
  - CT scan showed deep and superficial thrombi on LLE, thickening of fascial tissue, evidence of septic embolization to lung
- Assessment
  - Necrotizing fasciitis with venous thrombosis, septic embolization to lung
- Treatment:
  - Antimicrobials: Vanc, Zosyn, Ceftaz, Fluconazole
  - Surgical exploration and debridment L thigh



## Case 1- PICU Course HD2

- On return from OR - everything fell apart
  - Worsening hemodynamics despite
    - fluid resuscitation
    - high dose Epi + NE
  - Worsening respiratory status with hypoxemia refractory to
    - HFOV at high pressures
    - FIO<sub>2</sub> = 1.0,
    - NO = 20 ppm
  - Worsening lactic acidosis
  - Worsening DIC and coagulopathy
- 15:40 (~24 hours after presentation to ED)
  - Decision made to use ECMO



## Diagnosis/Treatment

- MRSA necrotizing fasciitis, septic thrombosis with embolization to lung
- Sites:
  - Multiple blood cultures (X 5 days)
  - Tissue culture
- Sensitivities:
  - Clinda (no inducible resistance)
  - Levofloxacin
  - Linezolid
  - Rifampin
  - Tetracycline
  - TMP/SMZ
  - Vancomycin
- Treatment:
  - ECMO
  - Antibiotics
    - Vancomycin
    - Rifampin
    - Clindamycin
    - Gentamicin
  - IVIg

## Case 1-PICU Course HD2-37

- Complicated ECMO course
- Massive pulmonary hemorrhage - lung white-out
  - Repeated bronchoscopy
  - Repeated intratracheal TPA
- Nosocomial infections
- Renal failure - dialysis
- Hepatic failure
- Died from MODS on HD 37

## Case 2 - History

- 17 yo female
- 2 d h/o L calf pain after swimming
- Increased posterior knee pain, nausea, emesis, fever (T=40.3°C) & chills, near-syncope
- 1 d PTA seen in ED
  - Fluids and pain meds given
  - X-rays taken
  - Blood work
    - ESR = 47
    - CRP = 172
    - WBC = 10.4
- R shoulder and rib pain with deep inspiration
- PMH/PSH - ovarian CA 4 yr ago treated with bilateral oophorectomy and chemotherapy, no recurrence
- FH - paternal GM and uncle with DVT (?PE) after trivial trauma

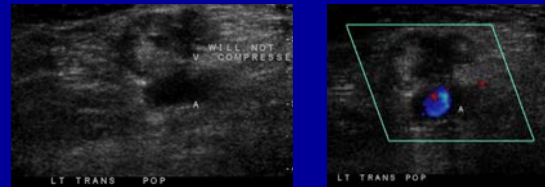
## Case 2 - Presenting PE

- In ED: (01:30)
  - T=38.7°C HR = 142 RR = 20 BP = 115/52 RA sat = 96% wt = 74 kg
  - Alert, cooperative
  - Tachycardic, normal pulses and perfusion
  - Clear lungs
  - L knee tender over popliteal region, slight swelling, no erythema, no Homan's sign
  - Limp with ambulation
- Labs
  - WBC = 12.2 with 51% segs, 41% bands
  - ESR = 57
- Treatment
  - 1 Liter IV fluid

## Case 2 - Course HD1

- On floor (06:00)
  - Afebrile, normal VS
  - Swollen L knee, slight warmth, no erythema, pain with flexion and extension
  - L calf tenderness with pain with dorsiflexion
  - Full ROM of hip
  - Tenderness to palpation over ribs, chest wall, R shoulder, scapula
- Ortho consult
  - Tapped knee - sympathetic effusion
- Treatment
  - IVF
  - Pain meds - Morphine, Tylenol, ibuprofen
- Studies
  - Ultrasound of popliteal vessels
  - CTA chest - r/o PE

## Case 2- Venous ultrasound



No PE on CTA  
Started on Lovenox

## Case 2 - Course HD2

- 09:00
  - Acute onset
    - SOB, chest pain
    - Hypoxemia requiring  $FiO_2 \sim 0.50$
    - Tachycardia (HR = 120's)
  - PICU consult and transferred to PICU
    - CTA chest - PE in R upper lung segment
    - Started on Vancomycin
    - BC from admission grew MRSA
      - Sensitive to
        - Clindamycin
        - Gentamicin
        - Levofloxacin
        - Linezolid
        - Rifampin
        - Tetracycline
        - TMP/SMZ
        - Vancomycin

## Case 2 - PICU Course

- PE
  - Persistent fever and tachycardia
  - Persistent hypoxemia
- Dx
  - Persistent positive BC - MRSA sepsis
  - Endocarditis ruled out
  - Work-up for cancer relapse negative
  - Work-up for thrombophilia negative
- Therapy
  - Vancomycin with trough >10
  - Rifampin added for 7 days
  - BiPAP, then intubation on HD 4 for desaturation, worsening lung disease
  - Lovenox
  - Dopamine for inotropic support

## Case 2 - PICU Course

- Developed anemia, cholestatic jaundice with normal LFTs
- Surgery and vascular surgery followed her for DVT with persistent sepsis
  - No surgical therapy indicated
- MRSA bacteremia until HD 8
- MRSA grew from trach aspirate
- Fever ( $T > 39^\circ C$ ) until HD 14
- Leukocytosis and bandemia until HD 27
- Usual PICU course, transferred to floor on HD 32
- Discharged home on HD 38

## Case 2

- Complications
  - Cholestatic jaundice - resolved
  - Renal insufficiency (BUN = 52, Creatinine = 1.8)
    - Discharge BUN = 10
    - Discharge creatinine = 1.6
  - Coag neg staph line infection
  - Pneumothorax requiring chest tube
  - Failed extubation on HD 23, successful extubation on HD 26
  - E. coli UTI on HD 32 treated with TMP/SMZ
  - Narcotic withdrawal syndrome treated with methadone
    - Resolved HD 38
  - Benzodiazepine withdrawal treated with lorazepam, then clonazepam
    - Resolved HD 38
  - Muscle weakness and decreased ROM
    - Required home PT/OT
    - Needed assistance to walk

## Summary of 2 Cases

- Recently healthy children
  - No association with hospital or health care workers
  - No history trauma
- Acute onset of LE pain  $\pm$  fever, leukocytosis with bandemia
- Rapidly deteriorating respiratory and/or hemodynamic status requiring PICU
- Invasive disease with septic thrombus and septic emboli to lung
- Destructive lung disease
- Clearance of MRSA and septic shock prolonged

## Staph aureus Virulence Factors

- Surface-associated proteins
  - Promote adhesion to damaged tissue
  - Promote adhesion to host cell surfaces
  - Bind proteins in blood - evade immune response
- Secrete extracellular enzymes (proteases, lipase, hyaluronidase, nuclease)
  - Facilitate tissue destruction
  - Promote spreading of organism
  - Damage host cell membranes
- Secrete toxins
  - Cause septic shock

## MRSA - History

- Pre-1940's
  - Staph infections serious
  - Bacteremia and pneumonia frequently fatal
- 1941 - era penicillin cure
- 1942
  - *Staph aureus* - penicillinases
- 1960 - era methicillin cure
- 1961
  - MRSA strains appeared
- 1960's - Vancomycin
  - MRSA strains disappeared

## MRSA - History

- 1980's - MRSA reappears
  - Associated exclusively with health-care facilities (HA-MRSA)
- 1990's -
  - HA-MRSA accelerates
  - CA-MRSA appearing
    - First in high-risk groups (caused by HA-MRSA strains)
      - IV drug abuser
      - LTC facilities
      - Patients with frequent healthcare contact
    - Previously healthy people with no risk factors
      - Predominately skin lesions (outbreaks)
      - Spread to other groups (outbreaks)
      - Nationally and internationally
      - Different genotype from HA-MRSA
  - 1997 - 1999 4 healthy children died (Minnesota, North Dakota)

## MRSA - History

- Late 1990's - early 2000's
  - CA-MRSA accelerating
  - Staph aureus develops
    - Inducible Clindamycin resistance
    - Vancomycin intermediate (VISA)
    - Vancomycin resistance (VRSA)
- Mid 2000's - present
  - Literature reports of Linezolid and daptomycin resistant strains
- CA-MRSA
  - not HA-MRSA that escaped
  - Genetically different
  - Clinically different

### Fifteen-Year Study of the Changing Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Crum et al. Am J Med 2006

Site of Infection	CA-MRSA (n=1044)	Nosocomial MRSA (n=457)	P value
Soft tissue/abscess	989 (95%)	218 (48%)	<.001
Urine	11 (1%)	56 (12%)	<.001
Sputum	4 (<1%)	87 (19%)	<.001
Blood	3 (<1%)	71 (16%)	<.001
Catheter/device	0 (0%)	52 (11%)	<.001
Ear/nose/sinus/throat	12 (1%)	12 (3%)	.04
CSF	0 (0%)	3 (<1%)	<.001
Other*	23 (2%)	19 (4%)	.04
Multiple sites	6 (<1%)	45 (10%)	<.001

\*eye, body fluids, vagina, bone, heart valves

### Fifteen-Year Study of the Changing Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Crum et al. Am J Med 2006

Site of Soft Tissue Infection	CA-MRSA (n=484)	Nosocomial MRSA (n=178)	P value
Extremity	338 (70%)	95 (53%)	<.001
Buttocks/genital	68 (14%)	18 (10%)	.20
Face/head/neck	35 (7%)	9 (5%)	.32
Trunk	43 (9%)	56 (32%)	<.001

- Cases increased from 10 in 1990 to 632 in 2004
- CA-MRSA
  - 16% hospitalized
  - 17% initially given appropriate antibiotic

### Fifteen-Year Study of the Changing Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Crum et al. Am J Med 2006

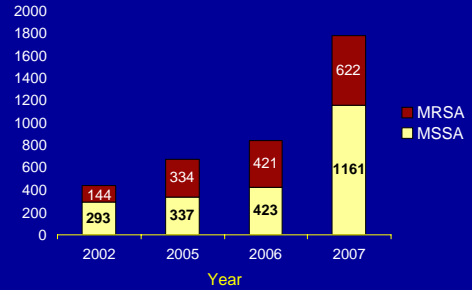
Factor	CA-MRSA (n=191)	Nosocomial MRSA (n=119)	P value
Age in years *	22 (0.5 - 87)	64 (0.5 - 99)	<.001
Male	145 (76%)	69 (58%)	.001
Medical History	17 (9%)	116 (98%)	<.001
# preexisting conditions *	0 (0 - 5)	3 (0 - 7)	<.001
Wound or device	6 (3%)	64 (61%)	<.001
Surgical history	5 (3%)	82 (70%)	<.001
Prior AB use	34/84 (41%)	63/84 (75%)	<.001
First AB effective	23/132 (17%)	23/53 (43%)	.001
Mortality	0 (0%)	23 (19%)	<.001

\*median (range)

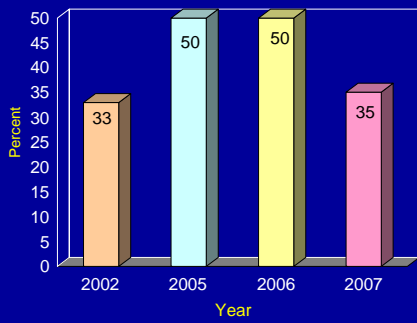
Fifteen-Year Study of the Changing Epidemiology of Methicillin-Resistant *Staphylococcus aureus*  
Crum et al. Am J Med 2006

Factor	CA-MRSA (n=191)	Nosocomial MRSA (n=119)	P value
Antibiotic Sensitivity			
Clindamycin	154/191 (81%)	21/112 (19%)	<.001
TMP/SMZ	183/186 (98%)	107/116 (94%)	.01
	(n=134)	(n=85)	
Panton-Valentine leukocidin +	93 (69%)	0 (0%)	<.001
Staph chromosome cassette type			
II	7 (5%)	80 (94%)	<.001
III	0 (0%)	3 (4%)	
IV	127 (95%)	2 (2%)	
Sequence Type			
1	15 (11%)	0 (0%)	<.001
5	7 (5%)	65 (77%)	
8	94 (70%)	1 (2%)	
30	11 (8%)	0 (0%)	
36	0 (0%)	9 (11%)	
59	5 (4%)	2 (2%)	

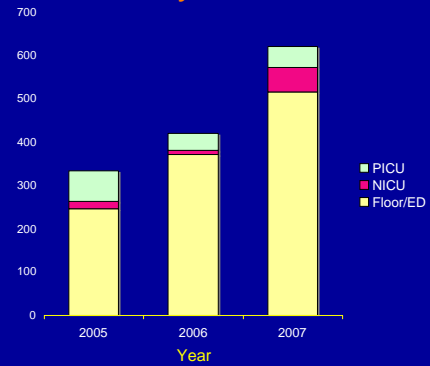
MRSA at CHOB



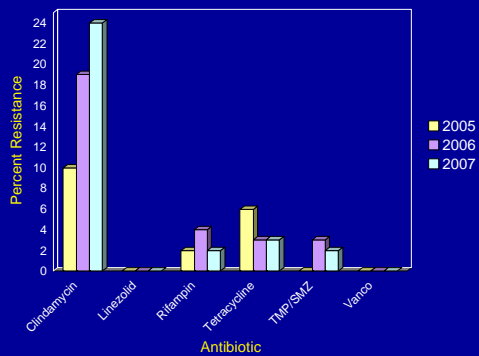
MRSA at CHOB



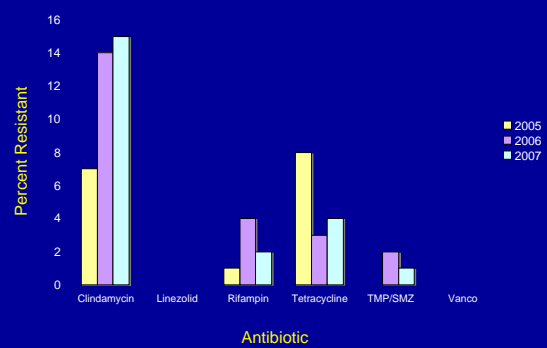
MRSA by CHOB Site



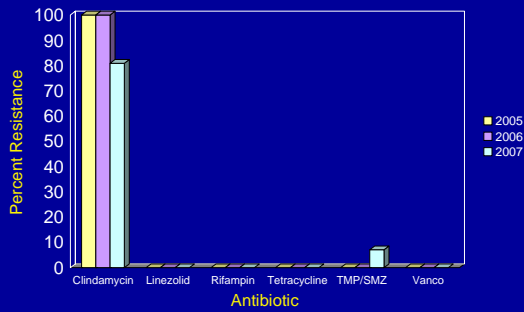
All CHOB MRSA Antibiotic Resistance



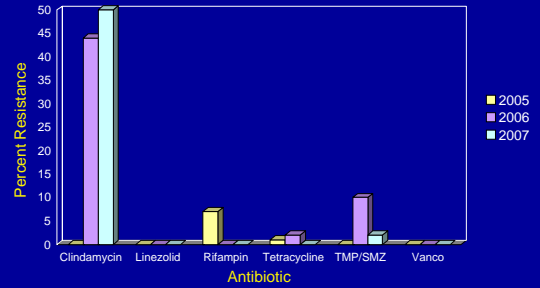
MRSA Antibiotic Resistance on CHOB Floor/ED



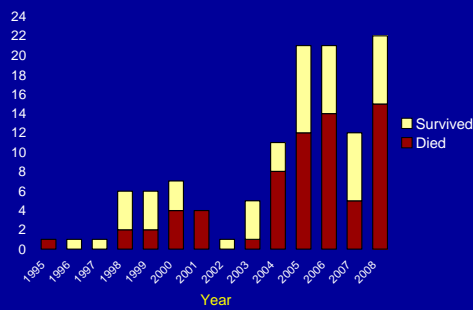
### MRSA Antibiotic Resistance in CHOB NICU



### MRSA Antibiotic Resistance in CHOB PICU



### ELSO data for MRSA Infections



### ELSO Data for MRSA Patients

Type of Support	Number	Died	% Mortality
Pulmonary	100	56	56
Cardiac	14	7	50
ECPR	5	5	100
All	119	68	57

### Summary

- MRSA
  - Increasing incidence (locally & nationally)
- CA-MRSA differs from HA-MRSA
  - Genome
  - Clinical syndromes
  - Therapeutic options
- CA-MRSA differs geographically
- CA-MRSA can cause serious illness

### Conclusion

*Staph aureus* is scary stuff  
and  
MRSA is the scariest of all!

## Any Questions?

### Special thanks to

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- Dr. Zahid Qureshi
- Patty Colosimo
- Kim Munschauer

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