Management of Methicillin-Resistant Staphylococcus Aureus Otitis

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Introduction

- Methicillin-resistant Staphylococcus aureus (MRSA) was initially detected in England in the 1960s
- Two strains
  - Community-associated strains (CA-MRSA): susceptible to commonly available antibiotics
  - Hospital-associated strains (HA-MRSA):

    multiple drug resistance, including vancomycin
- MRSA was isolated in 24% of specimens from suppurative otitis media in nationwide survey in Japan, November 1998 - March 1999

Journal of Infection and Chemotherapy 2003;9:46–52

Epidemiology

- Of cultures of ear infections:
  - MRSA: average in 7.0% (range 0.3 – 24.8%)
  - MSSA: average in 18.3% (range 9.6 – 32.1%)
  - Pseudomonas aeruginosa: in 36.6% (range 13.5 – 48.6%)

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Risk Factor - CA-MRSA infection

Previous MRSA infection or colonization
Residents of residential care facilities
Injection drug users
Patients who are HIV positive
Men who have sex with men
Patients with chronic skin disorders
Recurrent or recent antibiotic use
Low socioeconomic status

1. Journal of Antimicrobial Chemotherapy 2003;52:533–4
2. Journal of Hospital Infection 2006;63(Suppl 1):S1–44

Risk Factor - HA-MRSA infection

Hospitalization (overnight) in past 12 months
Surgery in past 12 months
Dialysis
Renal failure
Indwelling catheter or medical device
Residence in long-term care facility
Known colonization with MRSA in past 12 months

1. Journal of Antimicrobial Chemotherapy 2003;52:533–4
2. Journal of Hospital Infection 2006;63(Suppl 1):S1–44

Management

- Systemic antibiotic treatment
  - Parenteral therapy
  - Oral therapy
- Topical treatment
- Cleaning & Irrigation
- Surgery

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Systemic treatment

Concerning of antibiotic efficacy

- Current measure of efficacy of antibiotics: minimal inhibitory concentration (MIC) levels
- However, MIC is reflective of serum levels of antibiotics but not tissue levels

Systemic treatment

- Oral form in skin & soft tissue infection

Treatment	Adult dose	Pediatric dose
Clindamycin	300 to 450 mg orally three times daily	40 mg/kg/day in 3 or 4 doses
Trimethoprim-sulfamethoxazole	1 DS tab orally twice daily	8 to 12 mg trimethoprim component/kg /day in 2 doses
Doxycycline	100 mg orally twice daily	≤45 kg: 4 mg/kg/day in 2 doses >45 kg: 100 mg in 2doase
Minocycline	200 mg orally once, then 100 mg orally twice daily	4 mg/kg once, then 4 mg/kg/day in 2 doses
Linezolid	600 mg orally twice daily	<12 years: 30 mg/kg/day in 3 doses ≥12 years: 600 mg in 2 doses
Tedizolid	200 mg orrally once daily	

Clinical Infectious Diseases vol 52, No3, 2011 :pp 285-292

Systemic treatment

- Parenteral form in skin & soft tissue infection

Drug	Adult dose
Vancomycin	15-20 mg/kg/dose Q8-12H, max: 2 g per dose
Daptomycin	
Skin & soft tissue infection	4 mg/kg IV once daily
Bacteremia	6 mg/kg IV once daily
Linezolid	600 mg IV (or orally) twice daily
Ceftaroline	600 mg IV Q12H
Tigecycline	100 mg IV once, then 50 mg IV Q12H

1. Clinical Infectious Diseases , vol 49, 2009: pp177-80
2. Journal of Antimicrobial Chemotherapy, vol50, 2006:pp 3245-3249
3. Clinical Infectious Diseases , vol 52, No3, 2011 :pp 285-292

Guideline of antibiotics for otitis ?

- Guidelines for management of MRSA infections of skin and soft tissue had been established, but none for ear

Effective Treatment For Otitis from Literatures

- Parentral form
  Vancomycin: alone or combination to other agents

- Oral form
  Linezoid: alone
  TMP-SMX: alone or combination to other agents

Journal of Otolaryngology-Head & Neck Surgery,
Vol 38, No 4 (August), 2009: pp 483–494

Topical treatment

- Vancomycin
- Mupirocin
- Chloramphenicol

Topical treatment

J Laryngol Otol. 2004 Aug;118(8):645-7.

Topical vancomycin for chronic suppurative otitis media with methicillin-resistant Staphylococcus aureus otorrhoea.

Jang CH, Song CH, Wang PC.

Department of Otolaryngology, Wonkwang University Hospital, Wonkwang Medical School, Iksan, Korea. chulsavio@hanmail.net

- 55 chronic suppurative otitis media(CSOM) with MRSA otorrhea patients
- Treatment :
  - 35 patients with topical Vancomycin (25mg/ml), 2 drops (0.8 mg) 3 times daily for 10 days
  - 20 patients with topical gentamicin 0.3%, 2 drops 3 times daily for 10 days
- Result:
  - Vancomycin eardrops are effective in patients with MRSA otorrhea
  - No statistically significant difference in mean bone conduction thresholds after topical treatment

Topical treatment

Group	Ears (n)	Outcome, n (%)		
		Cure	Improvement	Failure
Vancomycin*	35	30 (85)	3 (8)	2 (5)
Gentamicin	20	2 (10)	2 (10)	16 (80)

*$p < 0.03$, vancomycin vs gentamicin

Topical treatment

Otol Neurotol. 2008 Aug;29(5):676-8. doi: 10.1097/MAO.0b013e31817ef4b7.

Clinical effectiveness of ototopical application of mupirocin ointment in methicillin-resistant Staphylococcus aureus otorrhea.

Furukawa M, Minekawa A, Haruyama T, Narui Y, Sugita G, Sugita R, Kusunoki T, Ikeda K.

Department of Otorhinolaryngology, Juntendo University School of Medicine, Tokyo, Japan.

- February 2006 - January 2007, 26 patients(13 COM & 13 post-operation) with MRSA otorrhea
- Treatment:
  - 16 patients with topical Mupirocin, 0.6gm 1-4 times for 2-3 weeks
  - 10 patients with ofloxacin ear drops, daily for 2 - 3 weeks
- Result:
  - Mupirocin are effective in patients with MRSA otorrhea
  - No significant difference in mean bone conduction thresholds after topical treatment

Topical treatment

Group	No. ears	Outcome (%)		
		Cure	Improvement	Failure
Mupirocin	18	18 (100)	0 (0)	0 (0)
Ofloxacin	10	2 (20)	2 (20)	6 (60)

Otology & Neurotology 2008;29:676–8

Topical treatment

Arch Otolaryngol Head Neck Surg. 2000 Dec;126(12):1440-3.

Methicillin-resistant Staphylococcus aureus otorrhea after tympanostomy tube placement: an emerging concern.

Hartnick CJ, Shott S, Willging JP, Myer CM 3rd.

Department of Pediatric Otolaryngology, Children's Hospital Medical Center, 3333 Burnet Ave, Cincinnati, OH 45229, USA. harq4k@chmcc.org

- December 1998-January 2000, 8 patients, ages of 1-11 years with COM and MRSA otorrhea
- Treatment & response :
  - Ciprofloxacin: 0/2
  - Chloramphenicol: 3/3
  - Tobramycin: 3/3

Possible Effective Alternative Topical Agents

- Fusidic acid — Clinical Otolaryngology and Allied Sciences 2001;26: 218–20; The Journal of Laryngology & Otology 2006;120:63–4
- Gentamicin — Archives of Otolaryngology - Head and Neck Surgery 2005;131: 782–4
- Gentian violet — Journal of Otolaryngology 2006;35:384–6

Aural cleaning & irrigation

Aural cleaning & irrigation

- Biofilms are the likely cause of CSOM & may resistance to antibiotic therapy

- Acetic acid including Burow's solution had a destructive effect on the biofilm of pathogens

1.ENT: Ear, Nose & Throat Journal
Aug 2002 Supplement 1, Vol. 81 Issue 8, p8-10
2. Archives of Dermatological Research
1999;/291:/570□3.

Aural cleaning & irrigation

Acta Otolaryngol. 2010;130(1):42-6. doi: 10.3109/00016480902870522.

The appropriate medical management of methicillin-resistant Staphylococcus aureus in chronic suppurative otitis media.

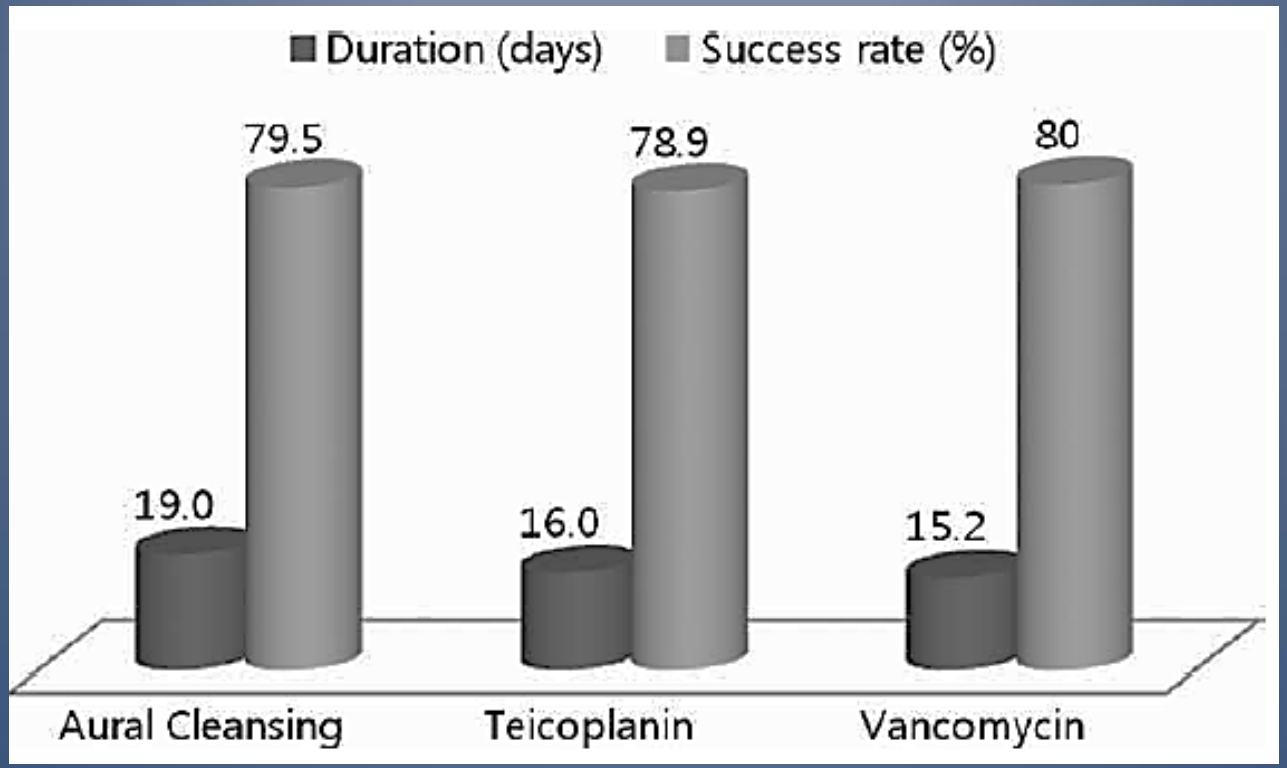
Choi HG, Park KH, Park SN, Jun BC, Lee DH, Yeo SW.

Department of Otolaryngology HNS, College of Medicine, Catholic University of Korea, Seoul, Korea.

- January 2005 - July 2008 of 85 patients with otorrhoea caused by CSOM, retrospectively
- Treatment modalities:
  - Aural cleansing & irrigation with diluted acetic acids (2 ml) (50 cases)
  - Intravenous Teicoplanin, 4 mg/kg (22 cases)
  - Intravenous Vancomycin, 20 mg/kg (15 cases)
- Result: no significant differences between the 3 groups

Acta Otolaryngol. 2010;130(1):42-6

Aural cleaning & irrigation



Acta Otolaryngol. 2010;130(1):42-6

Surgery

Surgery

Auris Nasus Larynx. 2007 Mar;34(1):9-13. Epub 2006 Aug 21.

Efficacy of mastoidectomy on MRSA-infected chronic otitis media with tympanic membrane perforation.

Mutoh T, Adachi O, Tsuji K, Okunaka M, Sakagami M.

Department of Otolaryngology, Hyogo College of Medicine, 1-1 Mukogawa, Nishinomiya City, Hyogo 663-8501, Japan. mutochin@hyo-med.ac.jp

- January 1998 - October 2003, 18 ears with surgery for MRSA-infected COM, 33 ears with surgery for MSSA-infected COM, retrospectively
- Treatment: tympanoplasty + mastoidectomy or tympanoplasty only
- Result: Mastoidectomy produced better results in discharging ears with MRSA-infected COM

Surgery

Characteristics of the patient group

		Total number of ears (patients)	M/F ratio	Average age in year (range)	Discharging /dry ears at operation
MRSA	Mastoidectomy	10(9)	3/7(0.43)	50.1(7-64)	9/1
	Non-mastoidectomy	8(8)	4/4(1.00)	47.3(6-64)	4/4
	Total	18(15)	7/11(0.64)	48.9(6-64)	13/5
MSSA	Mastoidectomy	11(10)	4/7(0.57)	49.0(32-71)	11/0
	Non- mastoidectomy	20(19)	7/13(0.54)	47.3(5-73)	15/5
	Total	31(28)	11/20(0.55)	47.9(6-64)	26/5

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Surgery

Graft success rates

		Discharging	Dry	Total
MRSA	Mastoidectomy	8/9(88.9%)	1/1(100%)	9/10(90.0%)
	Non-mastoidectomy	1/4(25.0%)	4/4(100%)	5/8(62.5%)
	Total	9/13(69.2%)	5/5(100%)	14/18(77.8%)
MSSA	Mastoidectomy	9/11(81.8%)	--------	9/11(81.8%)
	Non-mastoidectomy	12/15(80.0%)	4/5(80.0%)	16/20(80.0%)
	Total	21/26(80.8%)	4/5(80.0%)	25/31(80.6%)

Auris Nasus Larynx 34 (2007) 9–13

In Taiwan

In Taiwan

Acta Otolaryngol. 2002 Dec;122(8):827-30.

Community-acquired methicillin-resistant Staphylococcus aureus infections in discharging ears.

Hwang JH, Tsai HY, Liu TC.

Department of Otolaryngology, Poh-Ai Hospital, Lotung, Taiwan.

- August 2000 - February 2002, 248 isolates recovered from 221 discharging ears of patients

- Of cultures of ear infections:
  - MRSA: average in 12.2%
  - MSSA: average in 32.1%
  - Pseudomonas aeruginosa: in 34.4%

In Taiwan

Pathogen	Age (years)				
	< 20	21–40	41–60	>61	Total
MRSA	1 (3.7)	4 (14.8)	8 (29.6)	14 (51.9)	27 (100)
MSSA	7 (9.8)	30 (42.3)	18 (25.4)	16 (22.5)	71 (100)
Non-SA	22 (18.0)	25 (20.3)	34 (27.6)	42 (34.1)	123 (100)

Acta Otolaryngol 2002; 122: 827–830

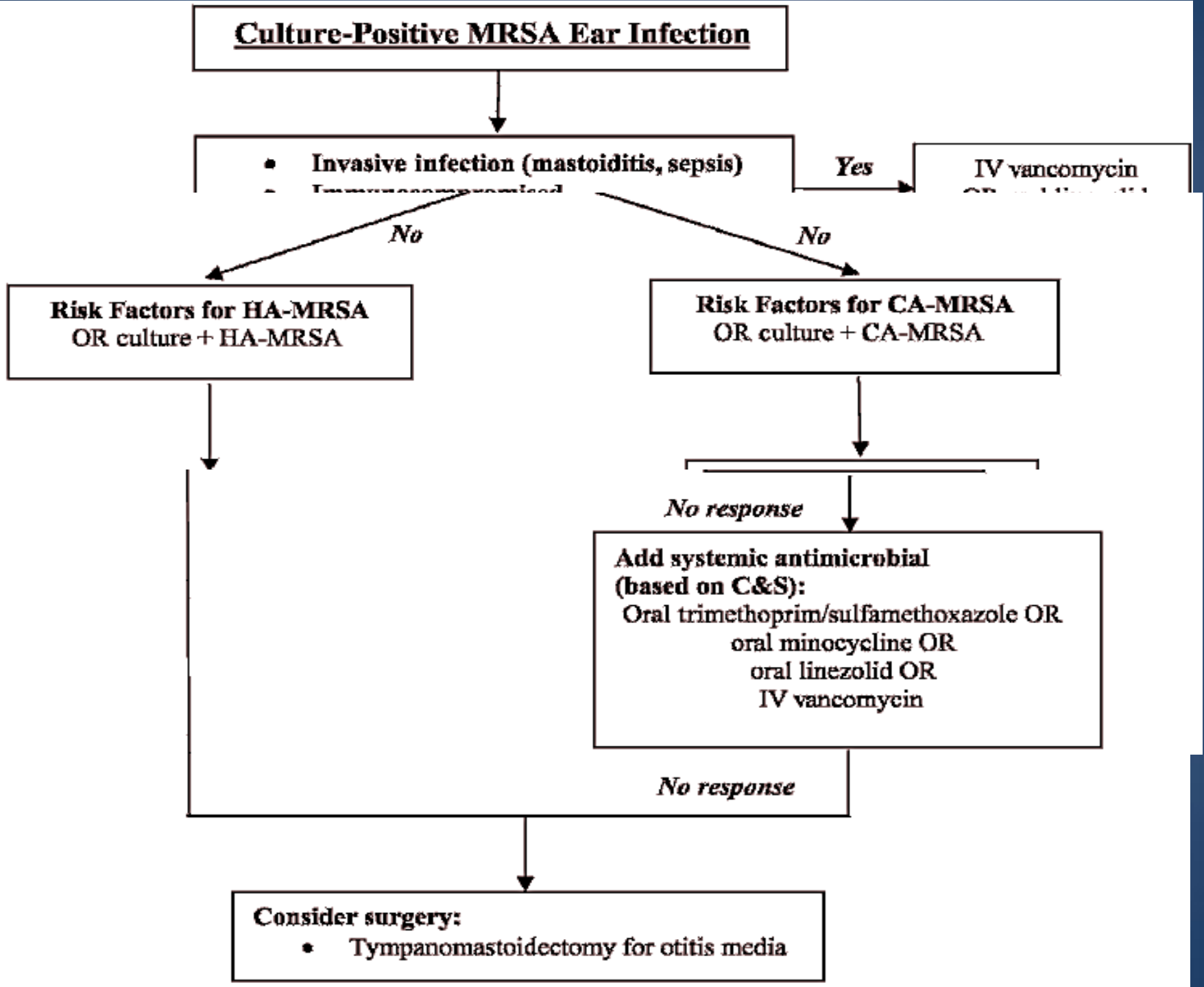
In Taiwan

Antibiotic	Susceptibility; n (%)
Vancomycin	27:27 (100%)
Teicoplanin	27:27 (100%)
Minocycline	26:27 (96.3%)
Fusidic acid	26:27 (96.3%)
Gentamicin	10:27 (37.0%)
Clindamycin	4:27 (14.8%)
Erythromycin	3:27 (11.1%)

Acta Otolaryngol 2002; 122: 827–830

Conclusion

- Systemic treatment
  - Parenteral therapy: Vancomycin: alone or with others
  - Oral therapy: Linezoid: alone
    TMP-SMX: alone or with others
- Topical treatment
  - Vancomycin ear drops
  - Mupirocin ointment
  - Chloramphenicol ear drops
- Cleaning & Irrigation
  - Diluted acetic acids
- Surgery
  - Tympanomastoidectomy


Culture-Positive MRSA Ear Infection
Invasive infection (mastoiditis, sepsis)
Yes
IV vancomycin
No
No
Risk Factors for HA-MRSA
OR culture + HA-MRSA
Risk Factors for CA-MRSA
OR culture + CA-MRSA
No response
Add systemic antimicrobial
(based on C&S):
Oral trimethoprim/sulfamethoxazole OR
oral minocycline OR
oral linezolid OR
IV vancomycin
No response
Consider surgery:
Tympanomastoidectomy for otitis media

Thanks for your listening