Methicillin resistant *Staphylococcus aureus*: is it a problem for nasal surgery?

A Sharma, C Philpott, L Pope, D McKiernan

Abstract

Methicillin resistant *Staphylococcus aureus* (MRSA) is becoming ever more prevalent in the UK, and the proportion of MRSA to methicillin sensitive *Staphylococcus aureus* (MSSA) seems to be increasing. New strains of MRSA are ever developing resistance to antibiotic treatment, increasing morbidity and mortality of infection.

Staphylococcus aureus is part of the normal flora of the nose, and MRSA colonizes the nose in infection. However, nasal surgery is rarely complicated by staphylococcal infections, and MRSA infection following nasal surgery is rare.

The authors present a literature review of MRSA infection, its relation to the nasal cavity, and infection following nasal surgery.

Key words: Methicillin; Staphylococcus aureus; Nose; Infection; Complication

Introduction

During the last two decades, methicillin resistant *Staphylococcus aureus* (MRSA) has become the most prevalent and important antimicrobial-resistant pathogen, causing serious nosocomial and community-acquired infections.¹

Background

Staphylococcus aureus is the cause of a vast array of illnesses, from relatively mild skin infections to deep abscesses, osteomyelitis, endocarditis, and bacteraemia, as well as staphylococcal toxic shock syndrome and food intoxication.² It was first described in the 1880s by Ogston, in Edinburgh, who found it was the most common cause of surgical wound infections.³

Before the introduction of penicillin in 1941, almost all *Staphylococcus aureus* were sensitive to penicillin but a few had the capacity to produce the enzyme penicillinase (or B-lactamase). Penicillinase broke down penicillin and provided the bacteria with resistance. By 1959, 90–95 per cent of clinical isolates were resistant to penicillin. They had been selected along Darwinian lines by the widespread use of penicillin.

Methicillin was the first B-lactam penicillin to be resistant to destruction by staphylococcal Blactamase. In 1961, within a year of the introduction of methicillin, the first MRSA was reported in England. MRSA was relatively uncommon before the 1970s, but the incidence increased in the 1980s, and exploded in the mid-1990s when particular epidemic strains of MRSA became established in hospitals in the UK.⁴

Methicillin resistant staphylococcus: the problem today

In the UK the number of infections from *Staphylococcus aureus* have risen during the past two decades.^{5,6} A study in England and Wales demonstrated that MRSA as a proportion of total *Staphylococcus aureus* bacteraemia rose from 2 per cent in 1990 to 34 per cent in 1998.⁷ By 2000 the proportion was 42 per cent, amongst the highest in Europe.^{8,9}

Bacteraemia of *Staphylococcus aureus*, has high mortality rates between 15 per cent and 60 per cent.^{10,11} With MRSA it is higher due to difficulties with reduced antimicrobial therapy, some of the agents are difficult to administer, have side effects, and may not penetrate particular body compartments well.⁸ Hospital-acquired MRSA may be less virulent than methicillin sensitive *Staphylococcus aureus* (MSSA) but is less responsive to antibiotics, increasing bed-stay, morbidity and mortality.

MRSA appears to be capable of acquiring resistance to virtually all clinically available compounds, including B-lactams, quinolones, streptogramin and the oxazolidinone group.¹² Glycopeptide

From the Department of Ear, Nose and Throat Surgery, Addenbrooke's NHS Trust, Cambridge and West Suffolk NHS Trust, Bury St. Edmunds, UK. Accepted for publication: 20 April 2006. 416

antimicrobials, notably vancomycin are presently the mainstay of treatment for MRSA. However, MRSA resistance to glycopeptides is developing.^{13–19} Clinically, Sakoulas reported a 44 per cent failure rate for MRSA bacteraemia²⁰ and Moise a 40 per cent failure in MRSA respiratory infections.²¹

Staphylococcus aureus is a nasal commensal

Staphylococcus aureus is a nasal commensal of the anterior nares of the nose. It is the most common organism to be cultured from nasal swabs.²² Interestingly, when the nares is treated topically to eliminate nasal carriage of staphylococcus, the organism is seen to disappear from other sites in the body.^{23,24}

A large proportion of the normal population carry MSSA. Around 60 per cent of people harbour *Staphylococcus aureus* intermittently. Around 20 per cent of the population almost never carry *Staphylococcus aureus*.²² Persistent carriage is more common in children, and many people change their pattern of carriage in puberty.²⁵ The reasons for persistent colonization patterns are unknown, but persistent colonization of other strains of *Staphyloccocus aureus*, at least during hospitalization.²⁶ The use of antibiotics in these persistent or intermittent carriers may cause elimination of MSSA and allow proliferation of MRSA.²⁷

It is assumed that most MRSA infections derive from nasal carriage,^{27–31} with the nose acting as the primary ecological reservoir of *Staphylococcus aureus* in humans.³² The incidence of nasal carriage of MRSA in patients on admission to intensive therapy units has been found to be 4.2 per cent.³³ In contrast, when patients already on intensive therapy units are swabbed the carriage rates are greater than 20 per cent.³⁴ In immunocompromised patients the nasal carriage rate is even higher.³⁰

Studies have shown that a few strains of *Staphylococcus aureus* are responsible for the majority of all infections.³⁵ It appears that the MRSA strains are spread more easily than the MSSA strains of *Staphylococcus aureus*.^{36,37}

It is thought that the actual carriage of MRSA by patients on hospital admission is higher than that found by MRSA positive swabs (i.e. it is more prevalent). MRSA carriage is more common in the elderly, particularly those in residential homes or rehabilitation units, and those with previous hospital admissions.³⁸ MRSA is not a problem in the healthy population of the general community.

Staphylococcus aureus infection in nasal surgery

Despite the obvious abundant colonization of the anterior nares with both MSSA and MRSA, infection following nasal surgery is rare. It has been suggested that half the patients who undergo septoplasty or rhinoplasty will be colonized with *Staphylococcus aureus*,³⁹ and, indeed, epidemiological studies of staphylococcus would also support this finding.²²

Infectious complications of *Staphylococcus aureus* following rhinology surgery include cellulitis,

sinusitis, septicaemia, cavernous sinus thrombosis, brain abscess, and toxic shock syndrome, but the rate of infection is less than 3 per cent,⁴⁰ with the incidence of toxic shock syndrome following nasal surgery being estimated at 0.0165 per cent⁴¹ (five in 1700 functional endoscopic sinus surgery (FESS) patients).⁴²

Prophylactic antibiotics in nasal surgery

Although the value of prophylactic antibiotics has been clearly demonstrated in head and neck surgery,⁴³ in nasal surgery there does not appear to be a role. Several studies have demonstrated no benefit from prophylactic antibiotics in nasal surgery.^{40,44–47} Indeed the use of prophylactic antibiotics has been demonstrated to decrease the natural flora e.g. diphtheroids, allowing proliferation of staphylococcus.⁴⁸ Administration of antibiotics does not prevent staphylococcus colonization and does not reduce the risk of toxic shock syndrome.³⁹

MRSA in nasal surgery

Staphylococcus aureus is a common cause of chronic sinusitis⁴⁹ and toxic shock syndrome.⁵⁰ There is little in the literature, however, as to the incidence of MRSA infections following nasal surgery.

Jiang *et al.*⁵¹ found the incidence of MRSA carriage post endoscopic sinus surgery to be 20.7 per cent, and MSSA 15.8 per cent, whereas in the patients with chronic sinusitis MRSA was seen in 3.5 per cent and MSSA in 16.9 per cent of the population. Interestingly, all patients received antibiotics for three to four weeks post-operatively, and the MRSA positive swabs were all cultured greater than 14 days post-operatively. This paper probably reflects how antibiotics change the natural flora of the nasal cavity, although the authors concluded that MRSA is more common post FESS per se.

Toxic shock syndrome caused by MRSA following nasal surgery has been described,^{52,53} but considering the number of endoscopic sinus surgical procedures performed worldwide the incidence is very low.

A review of the literature reveals no reported cases of MRSA infections following septoplasty or rhinoplasty. It would be expected that these infections would occur, as the surgical incision is made in a region of heavy staphylococcal growth, and increasingly the nosocomial staphylococcus strain is likely to be MRSA.

No studies are available to explain the lack of MRSA infection following nasal surgery. It may be that it is under diagnosed and under reported. However, we know the rate of MSSA infection following surgery is also low.⁴⁰⁻⁴²

Within our unit we are yet to see any cases of nasal surgery complicated by an MRSA infection, despite the incidence of MRSA being high within our hospital (0.36 cases per 1000 bed-days between April 2004 and September 2004), when compared to the national figures.⁵⁴

The risk of MRSA infection is dependent on a number of factors which include: patient population, type of surgery, location and use of systemic antibiotics.²² For example, MRSA is a problem in head and neck cancer patients,⁵⁵ who tend to be elderly, have prolonged periods of hospitalization, have high dose peri-operative antibiotics and are often immunocompromised.

One reason for MRSA infections not apparently complicating septal and rhinoplasty surgery, may be the age of the patient. They tend to be middle aged, medically fit and well, and therefore have relatively few admissions to hospital. Normally living in the community, they may not be exposed to the health care workers and residential home population, in whom MRSA incidence is higher. They also tend to have shorter admissions, often less than 24 hours. In the study by Jiang *et al.*⁵¹ patients were admitted for three to four days post-operatively, exposing them to possible gross infection by health care workers and other patients.

The general medical fitness of patients undergoing nasal surgery, and often lack of any debility, would make this population less likely to develop postoperative infections. They may also have had less antibiotic exposure than the elderly population of other surgeries, and the potentially protective normal flora of the nose, e.g. diphtheroids may be still present. They may also be persistent MSSA carriers (60 per cent of the normal population²²) who are found in the community, which may offer further protection against MRSA inoculation.

Another factor may be the high vascularity of the nose. This promotes healing of the surgical field, but also will allow the host defences to mount a good immune response against any potentially infecting organisms.

Conclusion

MRSA is becoming more prevalent, and the proportion of MRSA to MSSA seems to be increasing; but it is still uncommon amongst the healthy community, which includes those undergoing nasal surgery. As the proportion of MRSA to MSSA changes, we may yet see MRSA complicating nasal surgery rather than MSSA, but the rate of complication will remain low. However, the morbidity of an MRSA infection is likely to be higher because of the difficulty in treating MRSA due to its antibiotic resistance.

In future care may be required in prescribing antibiotics peri-operatively for nasal surgery. Such practice may potentially wipe out the natural nasal flora of MSSA, diphtheroids and other organisms, allowing MRSA to develop and flourish, in a population of patients that presently does not appear to be natural carriers. Inadvertently we may increase carriage of MRSA, and place our patients at risk of MRSA infection in the future.

References

- 1 Vos C, Verbrugh H. MRSA: We can overcome, but who will lead the battle? Infect Control Hosp Epidemiol 2005; 26:117-20
- 2 Lowy FD. Staphylococcus aureus infections. N Engl J Med 1998;339:520-32
- 3 Lyell A. Alexander Ogston (1844-1929)-staphylococci. Scott Med J 1977;22:277-8

- 4 Department of Health. A simple guide to MRSA. About methicillin resistant staphylococcus aureus. November http://www.dh.gov.uk/PolicyAndGuidance/Health AndSocialCareTopics/HealthcareAcquiredInfection/ HealthcareAcquiredGeneralInformation/Healthcare AcquiredGeneralArticle/fs/en?CONTENT_ID=4093113 &chk=7/XgcQ [20 April 2005]
- 5 National Nosocomial Infections Surveillance System report: data summary from January 1992–January 2001. Am J Infect Control 2001;29:404-21
- 6 Steinberg JP, Clark CC, Hackman BO. Nosocomial and community-acquired Staphylococcus aureus bacteremias from 1980 to 1993: impact of intravascular devices and methicillin resistance. Clin Infect Dis 1996:23:255-9
- Reacher MH, Shah A, Livermore DM, Wale MC, Graham C, Johnson AP et al. Bacteraemia and antibiotic resistance of its pathogens reported in England and Wales between 1990 and 1998: trend analysis. Br Med J 2000;320:213-16
- 8 Duckworth G. Controlling methicillin resistant staphylococcus aureus. *Br Med J* 2003;**327**:1177–8 Barrett SP, Spencer RC. MRSA bacteraemia surveillance
- scheme in England. *J Hosp Infect* 2002;**50**:241–2 10 Cluff LE, Reynolds RC, Page DL, Breckenridge JL. Staphylococcal bacteremia: demographic, clinical and microbiological features of 185 cases. Trans Am Clin Climatol Assoc 1968;79:205-15
- 11 Julander I, Svanbom M. Prediction of staphylococcal etiology among patients with septicemia with or without endocarditis by multivariate statistical methods. Scand J Infect Dis 1985;17:37-46
- 12 Wegner DL. No mercy for MRSA: treatment alternatives to vancomycin and linezolid. MLO Med Lab Obs 2005; 37:26-9
- 13 Chang S, Sievert DM, Hageman JC, Boulton ML, Tenover FC, Downes FP et al. Infection with vancomycin-resistant staphylococcus aureus containing the vanA resistance gene. N Engl J Med 2003;**348**:1342–7
- 14 Entenza JM, Que YA, Vouillamoz J, Glauser MP, Moreillon P. Efficacies of moxifloxacin, ciprofloxacin, and vancomycin against experimental endocarditis due to methicillin-resistant staphylococcus aureus expressing various degrees of ciprofloxacin resistance. Antimicrob Agents Chemother 2001;45:3076-83
- 15 Gonzalez-Zorn B, Courvalin P. VanA-mediated high level glycopeptide resistance in MRSA. Lancet Infect Dis 2003; 3.67-8
- 16 Malbruny B, Canu A, Bozdogan B, Fantin B, Zarrouk V, Dutka-Malen S et al. Resistance to quinupristin-dalfopristin due to mutation of L22 ribosomal protein in Staphylococcus aureus. Antimicrob Agents Chemôther 2002;46:2200-7
- 17 Moore MR, Perdreau-Remington F, Chambers HF. Vancomycin treatment failure associated with heterogeneous vancomycin-intermediate staphylococcus aureus in a patient with endocarditis and in the rabbit model of endocarditis. Antimicrob Agents Chemother 2003;47:1262-6 18 Pillai SK, Sakoulas G, Wennersten C, Eliopoulos GM,
- Moellering RC Jr, Ferraro MJ et al. Linezolid resistance in staphylococcus aureus: characterization and stability of resistant phenotype. J Infect Dis 2002;186:1603-7
- Solberg CO. Spread of staphylococcus aureus in hospitals: causes and prevention. *Scand J Infect Dis* 2000; 32:587-95
- 20 Sakoulas G, Moise-Broder PA, Schentag J, Forrest A, Moellering RC Jr, Eliopoulos GM. Relationship of MIC and bactericidal activity to efficacy of vancomycin for treatment of methicillin-resistant staphylococcus aureus bacteremia. J Clin Microbiol 2004;42:2398-402
- 21 Moise PA, Schentag JJ. Vancomycin treatment failures in staphylococcus aureus lower respiratory tract infections. Int J Antimicrob Agents 2000;16:31-4
- 22 Williams R. Healthy carriage of staphylococcus aureus, its prevalence and importance. Bacteriology Review 1963;27: 56 - 71
- 23 Parras F, Guerrero MC, Bouza E, Blazquez MJ, Moreno S, Menarguez MC et al. Comparative study of mupirocin and oral co-trimoxazole plus topical fusidic acid in eradication of nasal carriage of methicillin-resistant staphylococcus aureus. Antimicrob Agents Chemother 1995;39:175-9

- 24 Reagan DR, Doebbeling BN, Pfaller MA, Sheetz CT, Houston AK, Hollis RJ *et al.* Elimination of coincident staphylococcus aureus nasal and hand carriage with intranasal application of mupirocin calcium ointment. *Ann Intern Med* 1991;**114**:101–6
- 25 Armstrong-Esther CA. Carriage patterns of staphylococcus aureus in a healthy non-hospital population of adults and children. *Ann Hum Biol* 1976;**3**:221–7
- 26 Noble W, Williams R, Jevons M, Shooter RJCP. Some aspects of nasal carriage of staphylococci. 1964;17:79–83
- 27 Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of staphylococcus aureus: epidemiology, underlying mechanisms, and associated risks. *Clin Microbiol Rev* 1997;10: 505–20
- 28 Luzar MA, Coles GA, Faller B, Slingeneyer A, Dah GD, Briat C et al. staphylococcus aureus nasal carriage and infection in patients on continuous ambulatory peritoneal dialysis. N Engl J Med 1990;322:505–9
- 29 Yu VL, Goetz A, Wagener M, Smith PB, Rihs JD, Hanchett J et al. Staphylococcus aureus nasal carriage and infection in patients on hemodialysis. Efficacy of antibiotic prophylaxis. N Engl J Med 1986;315:91-6
- 30 Nguyen MH, Kauffman CA, Goodman RP, Squier C, Arbeit RD, Singh N et al. Nasal carriage of and infection with staphylococcus aureus in HIV-infected patients. Ann Intern Med 1999;130:221-5
- 31 von Eiff C, Becker K, Machka K, Stammer H, Peters G. Nasal carriage as a source of Staphylococcus aureus bacteremia. Study Group [see comment]. N Engl J Med 2001;344: 11–16
- 32 Moss B, Squire J, Topley E. Nose and skin carriage of staphylococcus aureus in patients receiving penicillin. *Lancet* 1948;1:320-5
- 33 Troche G, Joly LM, Guibert M, Zazzo JF. Detection and treatment of antibiotic-resistant bacterial carriage in a surgical intensive care unit: a 6-year prospective survey. *Infect Control Hosp Epidemiol* 2005;26:161–5
 34 Orsi GB, Raponi M, Franchi C, Rocco M, Mancini C,
- 34 Orsi GB, Raponi M, Franchi C, Rocco M, Mancini C, Venditti M. Surveillance and infection control in an intensive care unit. *Infect Control Hosp Epidemiol* 2005; 26:321–5
- 35 Koning S, van Belkum A, Snijders S, van Leeuwen W, Verbrugh H, Nouwen J *et al.* Severity of nonbullous staphylococcus aureus impetigo in children is associated with strains harboring genetic markers for exfoliative toxin B, Panton-Valentine leukocidin, and the multidrug resistance plasmid pSK41. *J Clin Microbiol* 2003;**41**:3017–21
- 36 Melles DC, Gorkink RF, Boelens HA, Snijders SV, Peeters JK, Moorhouse MJ *et al.* Natural population dynamics and expansion of pathogenic clones of Staphylococcus aureus. *J Clin Invest* 2004;**114**:1732–40
- 37 Vriens M, Blok H, Fluit A, Troelstra A, Van Der Werken C, Verhoef J. Costs associated with a strict policy to eradicate methicillin-resistant staphylococcus aureus in a Dutch University Medical Center: a 10-year survey. *European Journal of Clinical Microbiology & Infectious Diseases* 2002;21:782-6
- 38 Lucet JC, Grenet K, Armand-Lefevre L, Harnal M, Bouvet E, Regnier B et al. High prevalence of carriage of methicillin-resistant staphylococcus aureus at hospital admission in elderly patients: implications for infection control strategies. *Infect Control Hosp Epidemiol* 2005;26: 121-6
- 39 Jacobson JA, Stevens MH, Kasworm EM. Evaluation of single-dose cefazolin prophylaxis for toxic shock syndrome. Arch Otolaryngol Head Neck Surg 1988;114:326–7

- A SHARMA, C PHILPOTT, L POPE et al.
- 40 Weimert TA, Yoder MG. Antibiotics and nasal surgery. Laryngoscope 1980;90:667-72
- 41 Jacobson JA, Kasworm EM. Toxic shock syndrome after nasal surgery. Case reports and analysis of risk factors. *Arch Otolaryngol Head Neck Surg* 1986;**112**:329–32
 42 Abram AC, Bellian KT, Giles WJ, Gross CW. Toxic shock
- 42 Abram AC, Bellian KT, Giles WJ, Gross CW. Toxic shock syndrome after functional endonasal sinus surgery: an all or none phenomenon? *Laryngoscope* 1994;104:927–31
- 43 Johnson JT, Myers EN, Thearle PB, Sigler BA, Schramm VL Jr. Antimicrobial prophylaxis for contaminated head and neck surgery. *Laryngoscope* 1984;94:46–51
- 44 Strong MS. Wound infection in otolaryngologic surgery and the inexpediency of antibiotic prophylaxis. *Laryngoscope* 1963;**73**:165–84
- 45 Teichgraeber JF, Riley WB, Parks DH. Nasal surgery complications. *Plast Reconstr Surg* 1990;85:527–31
- 46 Lawson W, Kessler S, Biller HF. Unusual and fatal complications of rhinoplasty. Arch Otolaryngol 1983;109:164–9
- 47 Eschelman LT, Schleuning AJ 2nd, Brummett RE. Prophylactic antibiotics in otolaryngologic surgery: a double-blind study. *Trans Am Acad Ophthalmol Otolaryngol* 1971;**75**:387–94
- 48 Marples RR, Fulton JE, Leyden J, McGinley KJ. Effect of antibiotics on the nasal flora in acne patients. Arch Dermatol 1969;99:647–51
- 49 Brook I. Microbiology and management of sinusitis. J Otolaryngol 1996;25:249–56
- 50 Todd J, Fishaut M, Kapral F, Welch T. Toxic-shock syndrome associated with phage-group-I Staphylococci. *Lancet* 1978;2:1116–18
- 51 Jiang RS, Jang JW, Hsu CY. Post-functional endoscopic sinus surgery methicillin-resistant staphylococcus aureus sinusitis. Am J Rhinol 1999;13:273–7
- 52 Nakayama M, Tsunoda K, Igarashi M, Nishikawa K, Okazaki K. A case of toxic shock syndrome induced by MRSA after sinus surgery (in Japanese). *Masui* 1996;**45**: 994–7
- 53 Kanaya H. Toxic shock syndrome after nasal surgery Report of two cases. Otolaryngology. *Head and Neck Surgery (Tokyo)* 2005;77:55–59
 54 Health Promotions Agency Communicable Diseases
- 54 Health Promotions Agency Communicable Diseases Surveillance Centre for the Department of Health. Results of the first three and a half years of the Department of Health's mandatory methicillin resistant staphylococcus aureus (MRSA) surveillance system in acute Trusts in England. 2005 http://www.dh.gov.uk/PublicationsAnd Statistics/Publications/PublicationsStatistics/Publications StatisticsArticle [10 May 2005]
- 55 Watters K, O'Dwyer TP, Rowley H. Cost and morbidity of MRSA in head and neck cancer patients: what are the consequences? *J Laryngol Otol* 2004;**118**:694–9

Address for correspondence: Mr A Sharma, Dept of ENT Surgery, West Suffolk Hospital, Bury St Edmonds, Suffolk, IP33 2QZ, UK.

E-mail: aloksharma@mac.com

Mr A Sharma takes responsibility for the integrity of the content of the paper. Competing interests: None declared