Perspective

Tonsillectomy for persistent MRSA carriage in the throat—Description of three cases

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\textbf{A B S T R A C T}

In several countries, including the Netherlands, a search and destroy policy is part of the standard of care. Due to this policy and the restrictive use of antibiotics, the prevalence of methicillin-resistant \textit{Staphylococcus aureus} (MRSA) in the Netherlands – carrier state and infections – is among the lowest in the world. In the Netherlands, healthcare workers who are MRSA carriers are not allowed to perform work involving direct patient care. This means that treatment failure can have major implications for their working career. Despite repeated treatments according to guidelines, the eradication of MRSA fails in a minority of cases. It appears that performing a tonsillectomy can be part of the solution to this problem. As yet, tonsillectomy is not recommended as supplementary treatment for persistent MRSA carriage in the throat. There are a few expert opinions suggesting that tonsillectomy could possibly be helpful in decolonization. This article reports three recent cases in which MRSA eradication was successful only after tonsillectomy. It is believed that if eradication is necessary, tonsillectomy, if applicable, should be considered.

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\textbf{Introduction}

Approximately 20\% of healthy people are persistently colonized with \textit{Staphylococcus aureus}, most frequently in the anterior nares, but also at other body sites such as the perineum and throat. Another 30\% are intermittently colonized and the remaining 50\% appear to be non-susceptible to carriage (Ammerlaan et al., 2011a).

During the period 1999–2000, 0.03\% of Dutch patients admitted to hospital were found to be carrying MRSA on admission. This increased to 0.11\% during the years 2005–2007 (Wertheim et al., 2004; Bode et al., 2011). The European Antimicrobial Resistance Surveillance (EARS) network reported that in 2010, 1.2\% of the invasive \textit{S. aureus} isolates in the Netherlands were methicillin-resistant. This rate is significantly lower than those reported from other European countries like Belgium and Germany, where 21\% of the invasive isolates have been found to be methicillin-resistant (WIP (Werkgroep Infectie Preventie), 2012).

The prevalence of the methicillin-resistant \textit{Staphylococcus aureus} (MRSA) carrier state has mainly been studied in special populations such as patients at the time of admission, or patients on certain wards such as the intensive care unit. To achieve the highest detection rate of the prevalence of MRSA carriage, samples for culture should be obtained from different body sites, including the throat. In patients admitted to hospital, throat swabs were found to show the largest numbers of MRSA isolates among those not colonized at other sites (Bignardi and Lowes, 2009). In addition, throat carriage has been found to be nearly as common as nasal carriage (38\% versus 41\%) and much more common than perineal carriage (21\%). Among 17\% of patients, the throat was the only site where MRSA was detected. In patients in close contact with a known MRSA patient, 53\% were throat carriers of MRSA. Among 33\%, the throat was the only sample site with MRSA. In intensive care patients, throat carriage was found to be more frequent than either carriage in the nose or in the groin/axilla, and taking throat swabs from intensive care patients was found to significantly increase the detection rate of the MRSA carrier state (Marshall and Spelman, 2007; Batra et al., 2008; Jang et al., 2014). A recent review on multiple site surveillance for MRSA concluded that a combination of three swabs from different body sites results in the highest detection rate of MRSA colonization. The best combination
Table 1
Difference between uncomplicated and complicated MRSA carriage.

<table>
<thead>
<tr>
<th>Uncomplicated carriage</th>
<th>Complicated MRSA carriage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Individual without active infection with MRSA, and</td>
<td>• Carriage is located in the throat, perineal region, or skin lesions, independent of nasal carriage, and/or</td>
</tr>
<tr>
<td>• No active skin lesions, and</td>
<td>• Active skin lesions, and/or</td>
</tr>
<tr>
<td>• MRSA is sensitive in vitro to the antibiotic to be prescribed, and</td>
<td>• Foreign material that forms a connection between the internal and external environment, and/or</td>
</tr>
<tr>
<td>• No foreign material that forms a connection between the internal and the external environment (for example an external fixator), and</td>
<td>• MRSA is resistant to mupirocin in vitro, and/or</td>
</tr>
<tr>
<td>• Carriage is exclusively localized in the nose</td>
<td>• Previous treatments according to the recommendations for uncomplicated carriage have failed</td>
</tr>
</tbody>
</table>

MRSA, methicillin-resistant Staphylococcus aureus.

consisted of nasal and throat swabs combined with a swab from the groin or perineum or rectum (Chipolombwe et al., 2016).

In several countries, including the Netherlands, a search and destroy policy is part of the standard of care. Due to this policy and the restrictive use of antibiotics, the prevalence of MRSA in the Netherlands – carrier state and infections – is among the lowest in the world (Wertheim et al., 2004; Bode et al., 2011). The eradication of MRSA carriage yields two objectives: prevention of infection and prevention of transmission (Ammerlaan et al., 2011a). In the Netherlands, healthcare workers who are MRSA carriers are not allowed to perform work involving direct patient care. Therefore, all healthcare workers are offered eradication treatment for MRSA. This also means that treatment failure can have major implications for their working career.

Throat carriage of MRSA is important because it has been associated with treatment failure in the eradication of MRSA, among those with uncomplicated carriage and those with complicated carriage (Ammerlaan et al., 2011b). For some patients it may be desirable or even essential to achieve MRSA eradication. Tonsillectomy in patients with recurrent tonsillitis results in less frequent isolation of S. aureus strains from the throat (Katowska et al., 2017). In the case of failing eradication treatment due to persisting throat carriage, one could consider a tonsillectomy in order to achieve successful MRSA eradication.

The diagnosis of MRSA carriage requires the presence of S. aureus on the body surface and the presence of the mecA gene to be demonstrated. This gene encodes for the production of a modified penicillin-binding protein (PBP-2a). This protein has a lower affinity for beta-lactam antibiotics, which makes this group of antibiotics ineffective. Expression of the mecA gene is variable, thus detection can be difficult. An individual for whom MRSA is detected on the skin, mucosa, or foreign material is called a carrier. This is independent of the site of detection (nose, throat, perineal area) or amount detected (SWAB (Stichting Werkgroep Antibioticabeleid), 2012).

MRSA carriage can be divided into uncomplicated and complicated carriage (SWAB (Stichting Werkgroep Antibioticabeleid), 2012). The characteristics of each are described in Table 1. Colonization of the throat or perineal region (extra-nasal sites) or the presence of skin lesions is considered complicated carriage. The treatment of complicated and uncomplicated carriers differs. Among complicated carriers who have been treated according to guidelines, throat carriage and the presence of devices are associated with treatment failure (Ammerlaan et al., 2011b).

Treatment methods

The eradication of MRSA carriage yields two objectives: prevention of infection and prevention of transmission (Ammerlaan et al., 2011a). Treatment depends on the type of carriage. The Dutch Working Party on Antibiotic Policy – SWAB (Stichting Werkgroep Antibioticabeleid) – has formulated draft treatment guidelines for MRSA carriers (SWAB (Stichting Werkgroep Antibioticabeleid), 2012). In the case of uncomplicated carriage, local therapy with mupirocin ointment in the nose should be performed three times a day for 5 consecutive days. During these days, the subject’s hair should also be washed daily with disinfectant soap (chlorhexidine soap solution 40 mg/ml, or povidone iodine shampoo 75 mg/ml). Underwear, clothing, towels, and scrubs should be changed and washed each day. Bed linen has to be changed and washed on days 1, 3, and 5.

In the case of complicated carriage, any active skin lesions should be treated first, followed by systemic treatment for at least 7 days consisting of two antibiotics (Table 2), in addition to the treatment protocol for uncomplicated carriers.

Clinical cases

Case 1

An 18-year-old woman became colonized with MRSA during an outbreak of MRSA at the nursing home where she worked. This was a healthy individual, who used no medication or drugs and did not smoke. She had been treated previously at another hospital, initially with a combination of clarithromycin 600 mg three times daily and rifampicin 600 mg twice daily for 10 days, followed by a combination of doxycycline 100 mg twice daily and rifampicin 600 mg twice daily for 10 days. However, she continued to test positive for MRSA in the throat. Her parents and brother repeatedly tested negative. She was then treated with co-trimoxazole 960 mg twice daily and rifampicin 600 mg twice daily for 2 weeks. Consequently, she tested negative in cultures taken 3 and 10 days afterwards. However, she tested positive again in the third culture of the throat taken 17 days after treatment. All antibiotic treatments were combined with mupirocin nasal ointment three times daily and with daily washing with antibacterial soap. It was decided to perform a tonsillectomy. Cultures of the throat, nose, and perineum taken weekly for 6 weeks afterwards remained negative, as well as cultures taken after 5, 9, and 15 months.

Table 2
Systemic treatment for complicated carriage according to the SWAB guidelines.

<table>
<thead>
<tr>
<th>Antibiotic 1</th>
<th>Antibiotic 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preference</td>
<td></td>
</tr>
<tr>
<td>Doxycycline 200 mg QD e 1 dd 200 or Rifampicin 600 mg BID</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim 200 mg BID</td>
<td></td>
</tr>
<tr>
<td>Alternative</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin 500 mg BID or Fusidic acid 500 mg TID</td>
<td></td>
</tr>
<tr>
<td>Clindamycin 600 mg TID dd 600 or Ciprofloxacin 750 mg BID</td>
<td></td>
</tr>
<tr>
<td>Fusidic acid 500 mg TID</td>
<td></td>
</tr>
</tbody>
</table>

SWAB, Stichting Werkgroep Antibioticabeleid (The Dutch Working Party on Antibiotic Policy); dd, QD = ‘qua die’ means once a day; BID = ‘bis in die’ means two times a day, TID = ‘ter in die’ means three times a day.
Case 2

A 26-year-old medical student tested positive for MRSA including a throat culture. Her mother was a nurse who had tested negative. The student had no body piercings or skin diseases and did not use any medication. The first treatment consisted of rifampicin 600 mg twice daily and co-trimoxazole 960 mg twice daily in combination with mupirocin nasal ointment three times daily and daily washing with antibacterial soap for 1 week. However, a throat culture taken 3 days after treatment was still positive for MRSA. Subsequently she received the same treatment for 2 weeks, but with clindamycin 600 mg three times daily in place of the co-trimoxazole. Although the first culture taken after 3 days tested negative, the next throat culture taken 7 days later tested positive again. As she wished to work within the Dutch healthcare system, eradication of MRSA was necessary and a tonsillectomy was performed. Afterwards the throat culture was still positive. The same treatment (clindamycin and rifampicin) was then repeated for 1 week. Following this, she remained negative in three cultures taken at 3, 10, and 17 days after the operation, as well as 9 months later.

Case 3

A 37-year-old woman tested positive for MRSA. She worked in a healthcare facility for elderly people suffering from dementia. Her husband and daughter tested positive, as did her pet rabbit. The woman, daughter, and husband were all treated with co-trimoxazole 960 mg twice daily and rifampicin 600 mg twice daily in combination with mupirocin nasal ointment three times daily and daily washing with antibacterial soap for 1 week. The rabbit was treated with at least one course of antibiotics by a veterinarian. After treatment, cultures taken from the rabbit tested negative for MRSA. Initially the whole family tested negative, but then cultures from the 17-year-old daughter, taken 10 days and 17 days after treatment, were positive for the nose and throat, respectively. She received the same treatment for 2 weeks, replacing co-trimoxazole with clindamycin 600 mg three times daily. A throat culture 3 days after treatment was negative but the next culture, taken 1 week later, tested positive again. A tonsillectomy was performed, but she continued to harbour MRSA in the throat. The last treatment given was repeated for 1 week. Although her father became positive again after 1 year, the daughter never tested positive again for MRSA in seven cultures taken during a period extending from 3 days to 22 months after the last treatment.

Discussion

Approximately 20% of healthy people are persistently colonized with Staphylococcus aureus. Another 30% are intermittently colonized and the remaining 50% appear to be non-susceptible to carriage. Eradication treatment for MRSA depends on the type of carriage. MRSA carriage can be divided into uncomplicated and complicated carriage. In terms of localization, carriage is considered complicated when it is located in the throat or perineal region, or when there are skin lesions, independent of nasal carriage.

SWAB has drafted treatment guidelines for MRSA carriers, divided into local therapy of mupirocin ointment in the nose and disinfectant soap for uncomplicated carriage, and systemic treatment in the case of complicated carriage (SWAB (Stichting Werkgroep Antibiotica Beleid), 2012).

As it is known that transmission between household members can occur in about 50% of cases (Mollema et al., 2010) and carriage by household members is associated with treatment failure (Ammerlaan et al., 2011b), additional carriers in the same household should be treated simultaneously.

Ammerlaan et al. investigated the effectiveness of the SWAB guidelines. The first eradication treatment was successful in 60% of MRSA carriers. Of the patients whose first treatment failed, 62% were retreated according to guidelines, which increased the success rate to 80% with a median time of 10 days (Ammerlaan et al., 2011a). However, in a minority of cases, eradication treatment fails despite repeated treatments. Among complicated carriers treated according to guidelines, throat carriage and the presence of devices have been associated with treatment failure (Batra et al., 2008). For Dutch healthcare workers, this can have major implications for their working career. In the Netherlands, healthcare workers with the MRSA carrier state are not allowed to perform their work. Suspension from work is only ended when the employee has tested negative for MRSA three times (WIP (Werkgroep Infectie Preventie), 2012).

Kniehl et al. described treatment failure in efforts to decolonize MRSA contaminated healthcare workers. Treatment failure occurred in 4%, and recurrent colonization in 13% of cases (Kniehl et al., 2005). The failure of decolonization was ascribed to non-compliance, inadequate treatment, or massive environmental contamination. Furthermore, the advice was given to treat MRSA-positive household members.

In 2001, a case report was published in which a healthcare worker, who persistently tested positive for MRSA in the throat despite repeated eradication treatments, underwent a tonsillectomy. After tonsillectomy, the treatment of MRSA was successful (Leenders et al., 2001; Leenders et al., 2005). This previous case appears to be the only case in which tonsillectomy has been described as providing successful eradication of MRSA after several treatment failures. Expert opinions have suggested that it is possible that the tonsils could be a maintenance factor for MRSA carriage. Until now, tonsillectomy has not been recommended as a supplementary treatment for persistent MRSA carriage in the throat. There are a few expert opinions suggesting that tonsillectomy could possibly be helpful in decolonization.

Of all MRSA patients treated by the present authors over the past years, these three patients had a very significant motive for ending their MRSA carrier state. Due to the failure of successive treatments, the possibility of tonsillectomy was discussed as a last means of eradicating MRSA. Tonsillectomy itself does not always eradicate MRSA from the throat. After tonsillectomy, two of the three patients reported here continued to harbour MRSA in the throat. However, one course of antibiotic treatment after tonsillectomy was successful in eradicating MRSA from the throat in these cases. Although only three such cases have been seen in past years, tonsillectomy was successful in achieving eradication of the MRSA carrier state in all cases. This suggests that the presence of the tonsils could be the limiting factor for the eradication of MRSA in the throat.

In conclusion, eradication therapy for MRSA carriage sometimes fails due to the persistence of MRSA in the throat. In some patients, it can be desirable or even essential to achieve MRSA eradication. In the case of failing eradication treatment due to persisting throat carriage, one could consider a tonsillectomy in order to achieve successful MRSA eradication.

Conflict of interest

This article was not funded and there is no conflict of interest.

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