Original Article

Clinical Features Associated with Nasal *Staphylococcus aureus* Colonisation in Chinese Children with Moderate-to-severe Atopic Dermatitis

KLE Hon,[1] *MBBS, FAAP*, MCA Lam,[1] *BSc*, TF Leung,[1] *MBChB, MRCPCH, MD*, WYC Kam,[1] *BSC*, MCA Li ,[1] *BSc, MBBch, MRCP*, M Ip,[2] *MRCPath, FRCP, FRCPA*, TF Fok,[1] *MBBS, FRCP, MD*

Abstract

Introduction: *Staphylococcus aureus* colonisation/infection is common in children with atopic dermatitis (AD). Materials and Methods: We evaluated the nasal and body swabs of Chinese children with moderate-to-severe AD as assessed using SCORing-Atopic-Dermatitis (SCORAD) score. Swabs were taken from the right nostril, 5 flexural sites (anterior neck, antecubital fossae and popliteal fossae) and the skin area most severely affected (with oozing/crusting) for bacteriologic culture. Results: Fifty-five children (30 males and 25 females) were evaluated. Moderate-to-heavy growth of *S. aureus* was present in 12 (22%) of the nasal swabs, and in 1 or more flexural swabs of 32 (58%) of these children. Only 7 (35%) out of the 20 patients who had swabs taken from the worst skin area had moderate-to-heavy growth of *S. aureus*. Significant nasal *S. aureus* colonisation was associated with higher total ($P = 0.029$) and objective SCORAD scores ($P = 0.040$), more extensive disease ($P = 0.025$), the presence of oozing or crusting ($P = 0.023$) and higher eosinophil counts ($P = 0.038$). All specimens of methicillin-sensitive *S. aureus* were sensitive to cloxacillin and 71% to erythromycin. Methicillin-resistant *S. aureus* (MRSA), sensitive to vancomycin, was only isolated in 1 patient. Conclusions: In this study, *S. aureus* is a principal pathogen. Cloxacillin and first-generation cephalosporins have a favourable sensitivity profile even in children with moderate and severe atopic dermatitis. The anterior nares are an important harbour for *S. aureus* and significant nasal *S. aureus* colonisation was clinically associated with more extensive lesions and the presence of oozing or crusting.

Ann Acad Med Singapore 2005;34:602-5

Key words: Children, Flexures, Nose, SCORAD

Introduction

Atopic dermatitis (AD) is a common chronic relapsing disease in children. It was estimated that about 15% of children suffer from this disease.[1-3] Bacterial colonisation/infection due to *Staphylococcus aureus* is considered an important factor in the pathophysiology and mechanism involved in AD exacerbation.[4,5] We set out to (i) review the spectrum and antimicrobial sensitivity of bacteria present in patients with moderate-to-severe AD and (ii) evaluate if features of disease severity may predict bacterial colonisation/infection.

Materials and Methods

Swabs taken from anterior nares, flexures (anterior neck, antecubital fossae and popliteal fossae) and the worst affected skin areas (defined as lesional skin with oozing or crusting) of children with moderate-to-severe AD (objective SCORAD >15)[6] managed at the paediatric dermatology service of a university teaching hospital over a 6-month period were reviewed. Only standard nasal and the 5 flexural swabs were taken if oozing or crusting areas were not present. Nasal (360° twist of swab stick) and body (5 seconds of rubbing) swabs (COPAN Innovation, Italy) were taken by one of the 2 staff (LMCA and KWYC). Patients were excluded from the study if they suffered from other inflammatory dermatitides (such as psoriasis, seborrheic dermatitis, ichthyosis) or had been treated with systemic antibiotics (such as cloxacillin or erythromycin)

[1] Department of Paediatrics
[2] Department of Microbiology
The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR, China
Address for Reprints: Dr Kam-lun Ellis Hon, Department of Paediatrics, The Chinese University of Hong Kong, 6/F, Clinical Science Building, Prince of Wales Hospital, Shatin, Hong Kong SAR, China.
Email: ehon@cuhk.edu.hk

in the previous 4 weeks. Bacterial cultures of the swabs were carried out by standard laboratory techniques and sensitivity towards common antibiotics examined. Bacterial growth was classified as scanty ($<10^4$ colony-forming units per mL), moderate (10^4 to 10^5), or heavy ($>10^5$). We defined moderate-to-heavy growth as significant growth, and scanty or nil growth as negative. AD severity was assessed by 1 of the investigators (HKLE) with the SCORAD index.[7] Other investigations (such as eosinophil counts and IgE levels) were also recorded. The study was approved by the Clinical Research Ethics Committee of the University. Student *t*-test or Mann-Whitney U test was used to analyse quantitative traits, and chi-square test was used to compare proportions. All comparisons were 2-sided, and *P* values less than 0.05 were considered statistically significant.

Results

Fifty-eight Chinese children with AD had nasal and body swabs taken between April 2004 and October 2004. Three were excluded from analysis because of mild disease (objective SCORAD below 15). The patients had been treated with combinations of emollients, topical corticosteroids, oral antihistamines or topical antibiotic on an as-needed basis. Moderate-to-heavy growth of *S. aureus* was present in more than one-fifth of the 55 nasal swabs, and in 1 or more flexural swabs of 32 (58%) out of 55 subjects (Table 1). Twenty patients (36%) had lesional skin with oozing or crusting and significant growth of *S. aureus* was isolated in 35% of these children (Table 1). The odds ratios (95% confidence interval) for isolating *S. aureus* in oozing or crusting lesions were 4.98 (1.05 to 32.23) as compared to swabs at flexures ($P = 0.040$) and 9.14 (1.09 to 65.33) as compared to nasal swabs ($P = 0.005$). Of the 188 swabs with positive growth (both insignificant and significant) of methicillin-sensitive *S. aureus*, 100% were sensitive to cloxacillin and first-generation cephalosporins, 99.5% to co-trimoxazole, 71.3% to erythromycin and 75.5% to fusidic acid. Methicillin-resistant *S. aureus* (MRSA) was uncommon, found in 5 flexural, 1 nasal and 1 lesional specimens of 1 patient. All the 7 isolates were sensitive to vancomycin, but resistant to penicillins, cloxacillin, erythromycin, cephalosporins and carbapenems. Five of these isolates were sensitive to fusidic acid.

Significant nasal *S. aureus* colonisation was associated with higher total ($P = 0.029$) and objective SCORAD scores ($P = 0.040$), more extensive disease ($P = 0.025$), the presence of oozing or crusting ($P = 0.023$), and a higher eosinophil counts ($P = 0.038$) (Table 2). Moderate-to-heavy growth of *S. aureus* was isolated from the flexure(s) of 8 (67%) of the 12 patients with significant nasal growth and 24 (58%) of 43 patients with insignificant nasal growth ($P = 0.50$) When compared with insignificant flexural swabs, patients who had 1 or more flexural swabs with significant growth of *S. aureus* (n = 32) had higher mean (SD) SCORAD [63.9 (19.7) versus 53.6 (15.1), $P = 0.034$], more extensive disease [61.8 (24.7) % versus 49.5 (18.4) %, $P = 0.039$], and higher score for dryer skin [2.1 (0.8) versus 1.6 (0.8), $P = 0.038$].

Discussion

As documented in many studies, *S. aureus* is the most important pathogen associated with moderate-to-severe AD and the anterior nares may serve as an important reservoir.[4,5] Significant growth of coagulase-negative

Table 1. Bacteriology in the Nasal, Flexural (5 Samples Per Patient) and Lesional (Most Severely Affected Area with Oozing or Crusting) Swabs in 55 Children with Moderate-to-severe Atopic Dermatitis

Bacterial isolate	Sites of swab			*P*	
	Nasal (n = 55)	Flexural (n = 275)	Lesional (n = 20)	Moderate-to-heavy growth vs no to scanty	Any growth vs no growth
Staphylococcus aureus					
Moderate-to-heavy growth	11 (20)	65 (23)	7 (35)	0.482	0.007*
Scanty growth	10 (18)	62 (23)	9 (45)		
Coagulase-negative staphylococcus					
Moderate-to-heavy growth	2 (4)	14 (5)	1 (5)	0.359	0.208
Scanty growth	3 (5)	27 (10)	0		
Mixed bacterial growth					
Moderate-to-heavy growth	2 (4)	22 (8)	1 (5)	0.195	0.456
Scanty growth	2 (4)	4 (1)	0		
No growth	24 (44)	79 (29)	2 (10)		

Results were expressed as numbers (percentages).

Other organisms (*Diphtheroids*, alpha-haemolytic streptococci, *Bacillus species*, *Acinetobacter*) were isolated in only 5 (1%) of the 350 swab specimens.

* The odds ratios (95% confidence interval) for isolating *S. aureus* in oozing or crusting lesions were 4.98 (1.05 to 32.23) as compared to flexures ($P = 0.040$) and 9.14 (1.09 to 65.33) as compared to nasal swabs ($P = 0.005$).

Table 2. Characteristics of the 55 Children with Moderate-to-severe Atopic Dermatitis: Significant versus Negative Nasal Swabs

	Significant growth (n = 12)		Insignificant growth (n = 43)		*P*
Age (y)	12.0	(3.6)	11.8	(4.3)	0.853
Male gender [n (%)]	9	(75)	21	(49%)	0.108
SCORAD	69.8	(22.6)	56.7	(16.4)	0.029
Objective SCORAD	55.6	(19.5)	44.1	(16.0)	0.040
Extent, % body surface area	69.6	(25.4)	53.0	(21.1)	0.025
Intensity	11.9	(4.2)	9.5	(3.5)	0.104
Components under intensity					
Erythema	1.6	(1.1)	1.4	(1.1)	0.598
Oedema/papulation	2.3	(0.8)	1.9	(0.7)	0.133
Oozing/crust	1.9	(0.7)	1.2	(0.9)	0.023
Excoriation	2.3	(0.6)	1.9	(0.7)	0.122
Lichenification	1.7	(1.1)	1.4	(0.9)	0.341
Dryness	2.3	(1.0)	1.8	(0.8)	0.087
Pruritus	7.6	(1.8)	7.0	(1.7)	0.353
Sleep loss	6.6	(2.3)	5.6	(2.5)	0.385
IgE_{log}	3.64	(0.77)	3.32	(0.72)	0.224
Eosinophils in PB, %	12.6	(5.0)	9.0	(4.3)	0.038

IgE_{log}: log-transformed serum total IgE level; PB: peripheral blood; SD: standard deviation.
Results were expressed in mean (SD) unless stated otherwise.
"Significant growth" refers to moderate-to-heavy growth of *S. aureus*, and "insignificant growth" refers to nil or scanty growth.

staphylococcus was also found in a number of patients in this study, although it is usually regarded as a non-pathogenic skin commensal (Table 1). There was no information in the dermatology literature on this. Further study to evaluate if efforts to eliminate its presence in the skin (such as by regular topical antiseptic application) are associated with improvement of AD severity. Other organisms were only found in 1% of the cultures and contributed an insignificant role in this study. Even in the badly affected skin areas (defined as oozing or crusting), significant isolates of *S. aureus* was only found in approximately one-third of the specimens, which in part implies direct pathogen invasion may not be the sole factor in mediating AD. Acute exacerbations of eczema often present with oozing due to acute inflammation alone, but not infection. This occurrence is most significantly seen on the faces of young children. MRSA is uncommon. Most importantly, significant nasal or flexural *S. aureus* colonisation was associated with higher overall SCORAD scores and more extensive disease.

This study generates more questions than answers. First, where and how many swabs should we take in AD patients with extensive skin involvement? Hauser et al[8] reported that the frequency of *S. aureus* carriage was significantly higher in the apparently normal skin of AD patients than in healthy individuals. Compared to the normal skin of patients, *S. aureus* density was 100 to 1000 times higher in 3 different kinds of lesional skin (dermatitic, lichenified and impetiginised sites). We propose to take at least 2 swabs (1 nasal and 1 lesional) in each patient because (i) significant nasal growth is associated with higher SCORAD and more extensive disease, and (ii) lesions with oozing or crusting were associated with a high odds ratio of significant *S. aureus* isolation.

Enteral cloxacillin and erythromycin were the most often prescribed antibiotics for the empirical treatment of suspected bacterial infection in our clinic. In this study, all methicillin-sensitive *S. aureus* isolates were sensitive to cloxacillin but only 71.3% to erythromycin. We prefer cloxacillin or a first-generation cephalosporin to erythromycin as the first choice unless the patient has a history of penicillin allergy.

Second, would the eradication of *S. aureus* reduce SCORAD scores as well as eosinophil counts and serum IgE levels? Nasal *S. aureus* colonisation was associated with high eosinophil counts and IgE levels.[9] Specific IgE antibodies to staphylococcal enterotoxins have been identified in the serum of patients with AD.[10] Colonisation with superantigen-producing *S. aureus* is associated with increased severity of AD but superantigen production by *S. aureus* was inversely correlated with total IgE concentration.[11] We found that the SCORAD scores and eosinophil counts but not IgE levels were all significantly higher in children with significant ($\geq 10^4$ colony-forming units per mL) nasal carriage of *S. aureus*.

The study has some limitations. It did not confirm the pathogenic role of *S. aureus* since no comparison was made between the severity of atopic dermatitis before and after the eradication of the *S. aureus*. Besides, the numbers of patients included were small and there was no healthy control. Compared to the literature, the data on the growth of *S. aureus* are low. This may be due to the fact that the flexures were routinely swabbed and cultured regardless of

whether they were clinically colonised or infected.

In conclusion, this study confirmed that (i) *S. aureus* is an important pathogen among Chinese children with AD, (ii) cloxacillin has a favourable sensitivity profile for *S. aureus* even in Chinese children with moderate and severe AD, (iii) the anterior nares are an important harbour for *S. aureus* and significant nasal *S. aureus* colonisation was associated with higher total and objective SCORAD scores, more extensive lesions, the presence of oozing or crusting, and higher eosinophil counts. Therefore, we would recommend that cultures be considered not only in children with chronically extensive eczema, but also in children with an acute worsening of the extent or severity of their eczema.

REFERENCES

1. Foley P, Zuo Y, Plunkett A, Marks R. The frequency of common skin conditions in preschool-age children in Australia: atopic dermatitis. Arch Dermatol 2001;137:293-300.
2. Emerson RM, Williams HC, Allen BR. Severity distribution of atopic dermatitis in the community and its relationship to secondary referral. Br J Dermatol 1998;139:73-6.
3. Leung R, Wong G, Lau J, Ho A, Chan JK, Choy D, et al. Prevalence of asthma and allergy in Hong Kong schoolchildren: an ISAAC study. Eur Respir J 1997;10:354-60.
4. Williams JV, Vowels BR, Honig PJ, Leyden JJ. *S. aureus* isolation from the lesions, the hands, and the anterior nares of patients with atopic dermatitis. Pediatr Dermatol 1998;15:194-8.
5. Goodyear HM, Watson PJ, Egan SA, Price EH, Kenny PA, Harper JI. Skin microflora of atopic eczema in first time hospital attenders. Clin Exp Dermatol 1993;18:300-4.
6. Kunz B, Oranje AP, Labreze L, Stalder JF, Ring J, Taieb A. Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. Dermatology 1997;195:10-9.
7. Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology 1993;186:23-31.
8. Hauser C, Wuethrich B, Matter L, William JA, Sonnabend W, Schopfer K. *Staphylococcus aureus* skin colonization in atopic dermatitis patients. Dermatologica 1985;170:35-9.
9. Neuber K, Steinrucke K, Ring J. Staphylococcal enterotoxin B affects in vitro IgE synthesis, interferon-gamma, interleukin-4 and interleukin-5 production in atopic eczema. Int Arch Allergy Immunol 1995;107: 179-82.
10. Leung DY, Harbeck R, Bina P, Reiser RF, Yang E, Norris DA, et al. Presence of IgE antibodies to staphylococcal exotoxins on the skin of patients with atopic dermatitis. Evidence for a new group of allergens. J Clin Invest 1993;92:1374-80.
11. Zollner TM, Wichelhaus TA, Hartung A, Von Mallinckrodt C, Wagner TO, Brade V, et al. Colonization with superantigen-producing *Staphylococcus aureus* is associated with increased severity of atopic dermatitis. Clin Exp Allergy 2000;30:994-1000.