

Risk factors for severe impetiginized atopic dermatitis in Japan and assessment of its microbiological features

K. Hayakawa, K. Hirahara, T. Fukuda, M. Okazaki* and T. Shiohara

Department of Dermatology, Kyorin University School of Medicine, Mitaka, Tokyo, Japan; and *Department of Clinical Laboratories, Kyorin University Hospital, Mitaka, Tokyo, Japan

doi:10.1111/j.1365-2230.2008.03180.x

Summary

Patients with atopic dermatitis (AD) are susceptible to cutaneous bacterial infection. When such patients develop infection, some have extensive impetiginized dermatitis with high fever. To clarify the risk factors for severe impetiginized AD and its microbiological features, we reviewed clinical and microbiological data of 14 patients with impetiginized AD who were admitted to our hospital between the years 1999 and 2006. All patients had poorly controlled AD with eczematous lesions on the extensive body surface. The mean age was 28.2 years (range 18–35). Cultures of the lesional skin yielded both *Streptococcus pyogenes* and *Staphylococcus aureus* in 12 patients. *S. pyogenes* alone was isolated in two cases. These observations suggest that poorly controlled AD in adults is a risk factor for severe impetiginized AD and that *S. pyogenes* might play an important role in the development of severe clinical symptoms.

Patients with atopic dermatitis (AD) are susceptible to cutaneous bacterial infection.¹ Recent reports have shown that susceptibility to bacterial infection is closely related to the defect in innate immunity in patients with AD.^{2,3} When such patients are infected by bacteria, some develop extensive impetiginized dermatitis with high fever and general malaise, requiring immediate admission for treatment. However, there are few published reports on the risk factors for development of severe impetiginized AD and its microbiological features. To clarify these points, we reviewed the clinical data and microbiological findings in 14 patients with impetiginized AD who were admitted to our hospital.

Report

Patients with severe impetiginized AD were identified from admission hospital records in our hospital between

the years 1999 and 2006. There were 14 patients whose hospital records were detailed enough to assess the clinical and laboratory features. We reviewed their clinical data, the results of bacteriological cultures, and the results of T-antigen serological typing for *Streptococcus pyogenes* isolates.

The clinical and microbiological data of 14 inpatients with severe impetiginized AD are presented in Table 1. The average age was 28.2 years (range 18–35), and the disease was more common in men than in women, with a gender ratio of about 4 : 1. All patients were admitted to hospital on the day of presentation. Eleven patients had a high fever ($> 38^{\circ}\text{C}$) when they were hospitalized. The predilection sites were the face and limbs; the face was affected in 12 patients and the limbs in 9 patients, with 7 patients having both sites affected. Multiple pustules were seen in all cases (Fig. 1). Coexistent cellulitis was present in one patient (patient 13), and regional lymphadenitis in eight patients. The average white blood cell count was $14.9 \times 10^9/\text{L}$ (normal $3.5\text{--}9.0 \times 10^9$, with a cell count range of $9.3\text{--}20.6 \times 10^9/\text{L}$).

All 14 patients had poorly controlled AD, exhibiting eczematous lesions over extensive areas of the body. The diagnosis of AD was made according to the criteria of Hanifin and Rajka.⁴ At the time of admission, we could

Correspondence: Dr Kazuhito Hayakawa Department of Dermatology, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka, Tokyo, 181-8611, Japan.

E-mail: haykaz@kyorin-u.ac.jp

Conflict of interest: none declared.

Accepted for publication 6 August 2008

Table 1 Patient demographics and microbiological findings.

Patient	Age, years/ gender	BT (°C) on admission	WBC count ($\times 10^9$ /L) on admission	Affected area (impetiginized dermatitis)	Isolates from skin lesions	T serotype of <i>S. pyogenes</i>
1	26/M	38.2	14.4	Face, arms	<i>S. pyogenes</i> , <i>S. aureus</i>	B3264
2	21/M	38.3	20.6	Arms, legs	<i>S. pyogenes</i> , <i>S. aureus</i>	13
3	29/F	38.4	20.1	Face, neck, trunk	<i>S. pyogenes</i> , <i>S. aureus</i>	25
4	29/M	38.3	15.5	Face, arms, legs	<i>S. pyogenes</i> , <i>S. aureus</i>	25
5	35/M	39.1	13.0	Face	<i>S. pyogenes</i> , <i>S. aureus</i>	ND
6	35/M	39.5	16.8	Head, face	<i>S. pyogenes</i> , <i>S. aureus</i>	NT
7	24/M	38.4	9.3	Face, neck, arms	<i>S. pyogenes</i>	ND
8	18/F	39.4	13.9	Face, neck,	<i>S. pyogenes</i> , <i>S. aureus</i>	13
9	29/M	37.4	18.0	Face, arms, legs	<i>S. pyogenes</i>	28
10	29/M	38.0	12.6	Head, face, neck	<i>S. pyogenes</i> , <i>S. aureus</i>	13
11	27/M	37.8	17.7	Face, trunk, arms	<i>S. pyogenes</i> , <i>S. aureus</i>	13
12	33/M	38.8	11.0	Face, arms	<i>S. pyogenes</i> , <i>S. aureus</i>	4
13	35/F	37.0	13.3	Arms, legs	<i>S. pyogenes</i> , <i>S. aureus</i>	28
14	25/M	39.0	12.3	Face, arms	<i>S. pyogenes</i> , <i>S. aureus</i>	12

BT, body temperature; ND, not determined; NT, not typeable; *S. aureus*, *Staphylococcus aureus*; *S. pyogenes*, *Streptococcus pyogenes*; WBC, white blood cell.

**Figure 1** Patient 12, showing multiple, confluent pustules on the face.

not assess the patients' AD severity based on a clinical scoring system such as the SCORing Atopic Dermatitis (SCORAD) Index,⁵ because it was difficult to distinguish between the skin changes caused by AD and those caused by the bacterial infection. Four patients had not been treated for > 2 years, with a fear of steroids being the main reason for those patients being reluctant to receive treatment.

Antibiotics were given to all 14 patients, producing rapid resolution of the bacterial infection. Systemic corticosteroids were not given, but we used topical corticosteroids for the eczematous lesions in 12 patients.

Cultures of the pustules or erosions grew both *S. pyogenes* and *Staphylococcus aureus* in 12 patients, the latter being methicillin-sensitive in all cases. *S. pyogenes* alone was isolated in two cases. T-antigen serological typing of *S. pyogenes* isolates obtained from skin lesions was performed in 12 cases. T13 strains were most prevalent, being recovered in four cases. T25 and T28 types were recovered in two cases each. In all 13 patients, direct fluorescent antibody testing for herpes simplex virus (HSV) at the lesional sites and/or determination of serum anti-HSV antibodies at both acute and convalescent stage were performed. The results were negative or not significant in all, excluding concomitant HSV infection.

Our observations show that AD was poorly controlled in all 14 patients who were admitted to our hospital because of severe impetiginized dermatitis. Four patients had not received any treatment for > 2 years, as they had a phobia about steroids. Interestingly, the patients were all adults. People who visit our hospital for admission treatment belong to a wide range of age groups, including a large number of children. Accordingly, the fact that in this series, adults were affected exclusively could not be explained by bias in age of the patients who were hospitalized. Thus, it seems to be unquestionable that poorly controlled AD in adults is an important risk factor for severe impetiginized dermatitis. In uncontrolled AD, the skin barrier function becomes disrupted, with exudation of plasma proteins including profuse extracellular matrix proteins such as fibronectin. These proteins mediate adherence of Gram-positive bacteria to epithelial cells, and invasion into the cells,⁶

which might lead to spreading of a superficial bacterial skin infection over an extensive body area. The reason that the patients were all adults remains to be clarified. We can speculate that whereas parents usually take care of young children, preventing their AD from becoming serious, some adult patients who are reluctant to receive medical treatment including topical corticosteroid allow extreme exacerbation of their AD. This might make them particularly susceptible to bacterial skin infection. Another possibility is that streptococcal pharyngitis much more frequently affects children than adults,⁷ and consequently, children may have more effective immunity than adults to streptococci.

Cultures of skin lesions yielded *S. pyogenes* in all 14 cases, *S. aureus* being isolated concomitantly in 12 patients. We can speculate that *S. pyogenes* might play an important role in development of severe infection in our patients. However, how these two genera are related in the pathogenesis of impetiginized dermatitis in patients with AD remains to be elucidated. T-antigen serological typing of the isolates obtained from the skin lesions revealed that T13, T25, and T28 were relatively prevalent, accounting together for 66.7% of the 12 isolates examined. Although the function of T antigen remains to be clarified, it has been recently suggested that it could work as a virulence factor *in vivo*.⁸ Our results are similar to those reported by Fiorentino *et al.*,⁹ who showed that when *S. pyogenes* isolates, showing that when strains with certain emm patterns, which are the most common patterns found in impetigo strains, were examined for T serotypes, the

serotypes T13, T11, T25 and T28 were the most prevalent.

References

- 1 Leung DY. Infection in atopic dermatitis. *Curr Opin Pediatr* 2003; **15**: 399–404.
- 2 McGirt LY, Beck LA. Innate immune defects in atopic dermatitis. *J Allergy Clin Immunol* 2006; **118**: 202–8.
- 3 Hasannejad H, Takahashi R, Kimishima M *et al*. Selective impairment of Toll-like receptor 2-mediated proinflammatory cytokine production by monocytes from patients with atopic dermatitis. *J Allergy Clin Immunol* 2007; **120**: 69–75.
- 4 Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol* 1980; **92**: 40–7.
- 5 European Task Force on Atopic Dermatitis. Severity scoring of atopic dermatitis: the SCORAD index (Consensus Report of the European Task Force on Atopic Dermatitis). *Dermatology* 1993; **186**: 23–31.
- 6 Terao Y, Kawabata S, Kunitomo E *et al*. Fba, a novel fibronectin-binding protein from *Streptococcus pyogenes*, promotes bacterial entry into epithelial cells, and the fba gene is positively transcribed under the Mga regulator. *Mol Microbiol* 2001; **42**: 75–86.
- 7 Cunningham MW. Pathogenesis of group A streptococcal infections. *Clin Microbiol Rev* 2000; **13**: 470–511.
- 8 Lizano S, Luo F, Bessen DE. Role of streptococcal T antigens in superficial skin infection. *J Bacteriol* 2007; **189**: 1426–34.
- 9 Fiorentino TR, Beall B, Mshar P *et al*. A genetic-based evaluation of the principal tissue reservoir for group A streptococci isolated from normally sterile sites. *J Infect Dis* 1997; **176**: 177–82.