Clinical Manifestations of Skin and Soft Tissue Infections Including Cellulitis in Children

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Objective: The clinical manifestations of skin and soft tissue infections, including facial and non-facial cellulitis, have not yet been characterized in detail in children. The purpose of the present study was to elucidate the clinical manifestations of skin and soft tissue infections in children with facial and non-facial cellulitis.

Materials and Methods: This retrospective study reviewed the management of children with skin and soft tissue infections, including cellulitis, who were admitted to Sagamihara Kyodo Hospital between January 2001 and December 2013. Exclusion criteria were patients with immunosuppression, surgical site infections, and missing medical records.

Results: Data from twenty patients (10 males and 10 females) in the facial group and 25 (16 males and 9 females) in the non-facial group were analyzed. No significant differences were observed in the median age (interquartile range) at admission between the groups: 3.9 years (1.6–7.7 years) and 4.2 years (0.9–7.9 years) in the facial and non-facial groups, respectively. In the facial group, most patients were admitted between October and April (85%), whereas those in the non-facial group were mainly admitted between April and August (72%). No significant differences were observed in blood examination findings between the groups. Pus cultures were performed on discharges collected using needle aspiration in 14 patients. Methicillin-sensitive *Staphylococcus aureus* (MSSA) was isolated from 7 patients and *Streptococcus pyogenes* and coagulase-negative *staphylococci* from 2 patients. Penicillin-sensitive *S. pneumoniae* was isolated from 1 out of 24 patients (4%) for whom blood cultures were performed.

Conclusions: These results suggest seasonal differences in admissions, but minimal differences in clinical manifestations between the groups.

Key words: cellulitis, children, clinical manifestation, season, skin and soft tissue infections

Abbreviations

CEZ: cefazolin; CNS: coagulase-negative *staphylococci*; CRP: C-reactive protein; IDSA: Infectious Diseases Society of America; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-resistant *S. aureus*; SBT/ABPC: sulbactam/ampicillin; WBC: white blood cell

Introduction

Skin and soft tissue infections, including cellulitis, are common diseases that occasionally require hospitalization. These infections are classified by acute purulent inflammation, with greater depths being indicative of more severe infections. The prognoses of deep soft tissue infection and skin inflammation largely depend on the rapidity of the diagnosis and treatment initiation. The latter primarily involves radical surgical excision and appropriate antibiotic therapy. Lesions are deeper than erysipelas and lack a sharp demarcation from uninvolved skin. Erysipelas is raised above the level of the surrounding skin, with a clear line of demarcation between involved and uninvolved tissue. Bacterial invasion often results from disruption of the cutaneous barrier, and lymphedema and venous insufficiency are risk factors for cellulitis.

Cellulitis is mainly observed on the lower extremities, but may occasionally occur on the face. However, the distinction between clinical...
manifestations of facial and non-facial cellulitis in Japanese children remains unclear. Furthermore, studies to investigate differences in the clinical manifestations and bacterial pathologies of facial and non-facial pediatric cellulitis have not yet been conducted. Therefore, the purpose of the present study was to use a retrospective study design to elucidate clinical manifestations in children with facial and non-facial cellulitis.

Materials and Methods

1. Patient population and clinical information

We retrospectively reviewed the medical records of children with skin and soft tissue infections, including cellulitis, who were admitted to Sagamihara Kyodo Hospital between January 2001 and December 2013. The criteria for admission were periorbital swelling, visual disorders, systemic unwellness, or central signs or symptoms. The disease was defined as a skin infection with the acute development of an expanding area of erythematous lesions with swelling or pain. In the present study, erysipelas was defined as skin and soft tissue infections because it was difficult to differentially diagnose it from cellulitis. The facial group included children with infections of the head and face, while the non-facial group included children with infections of the neck, trunk, or extremities. The variables analyzed in this study included gender, gestational age, birth weight, the delivery method, and number of siblings. Exclusion criteria in this study for analyzing healthy patients only were patients with immunosuppression, surgical site infections, and missing medical records. Clinical information included the site of infection, use of oral antibiotics before hospital admission, duration between the appearance of local symptoms and time of admission, age and body temperature at admission, admission month, length of hospital stay, blood culture, types of antibiotics, and the duration of administration. Local symptoms were defined as the appearance of swelling and pain. Patients were discharged when acute phase reactants, such as C-reactive protein (CRP), almost improved to normal levels and the local site reaction disappeared.

2. Blood examination and imaging analysis

Blood samples obtained from patients with skin and soft tissue infections were analyzed for white blood cell (WBC) and neutrophil counts, and CRP levels were compared between the facial and non-facial groups at admission. CT and MRI findings that were useful for reaching a diagnosis and surgical consultations were compared between the two groups. CT and MRI were performed to define the extent of infection in the periorbital region and simultaneously assess the sinuses and abscess formation.

3. Bacteriological characteristics

The blood volume in the pediatric blood culture bottle was 1-4 mL (Sysmex bioMérieux Co., Ltd.). The culture was performed only once at the time of admission, and only one culture set was used in this study. Needle aspiration was performed based on the judgment of a surgical specialist for patients with a suspected abscess, and a pus culture was performed on the discharge collected using needle aspiration.

4. Treatment

The patients in the present study were empirically treated with intravenous antibiotics. Intravenous antibiotic treatments with a standard dosage for children were terminated when CRP improved to almost normal levels, and local symptoms disappeared. Thereafter, oral antibiotics were administered for 5-7 days.

5. Statistical analysis

Data were analyzed using GraphPad Prism for Windows version 5 (GraphPad Software, La Jolla, CA, USA). Data were presented as medians (interquartile range). Parameters between the groups were compared using the chi-squared and Mann-Whitney U tests. A p-value of < 0.05 was considered to be significant.

Results

1. Patient backgrounds and clinical information

Forty-five children with skin and soft tissue infections met the inclusion criteria. There were 20 patients (10 males and 10 females) in the facial group and 25 (16 males and 9 females) in the non-facial group. Median ages at admission were 3.9 years (1.6-7.7 years) and 4.2 years (0.9-7.9 years) in the facial and non-facial groups,
respectively; no significant difference was observed between the groups. There were also no significant differences in patient backgrounds or clinical information. None of the patients had skin or soft tissue infections during hospitalization in this study (Table 1). Regarding the age distribution, the facial group included a larger number of patients who were <10 years (85%). The non-facial group consisted of 1.9-fold more patients aged ≥10 years than in the facial group (p=0.47).

### Table 1 Patient backgrounds and clinical information

| Patient background                  | Facial group (n=20) | Non-facial group (n=25) | p-value |
|------------------------------------|--------------------|-------------------------|---------|
| Male                               | 10 (50)            | 16 (64)                 | 0.34    |
| Gestational age (weeks)            | 40 (39 – 40)       | 39 (39 – 41)            | 0.54    |
| Birth weight (g)                   | 2,835 (2,726 – 3,115) | 3,119 (2,954 – 3,446) | 0.10    |
| Normal delivery                    | 15 (75)            | 19 (76)                 | 0.46    |
| Siblings (numbers)                 | 2 (2 – 3)          | 2 (1 – 3)               | 0.53    |
| Admission age (years)              | 3.9 (1.6 – 7.9)    | 4.2 (0.9 – 7.9)         | 0.53    |

**Clinical information**

|                | Facial group | Non-facial group | p-value |
|----------------|--------------|------------------|---------|
| Swollen        | 20 (100)     | 24 (96)          | 0.37    |
| Pain           | 15 (75)      | 23 (92)          | 0.23    |
| Duration from local symptoms to admission (days) | 1 (0.8 – 2) | 2 (1 – 2) | 0.55 |
| Body temperature (℃) | 38.9 (37.8 – 39.2) | 38.5 (38.0 – 39.3) | 0.52 |
| Preadmission antibiotics | 6 (30) | 7 (28) | 0.88 |
| Length of admission (days) | 6 (4 – 7) | 6 (6 – 8) | 0.27 |

Data are expressed as a no. (%) or median (interquartile range). Facial group vs. non-facial group. Mann-Whitney U-test: gestational age, birth weight, siblings, duration from local symptoms to admission, admission age, body temperature, and length of admission. Chi-squared test: male, normal delivery, swollen, pain, and preadmission antibiotics. p-values of <0.05 were considered to indicate a significant difference.

**Figure 1**

Distribution of admission ages (n=45).

- Facial group
- Non-facial group

The facial group included a larger number of patients who were aged <10 years (85%). The non-facial group consisted of 1.9-fold more patients aged ≥10 years than in the facial group (p=0.47).
years old (85%), whereas the non-facial group consisted of 1.9-fold more patients ≥10 years old than in the facial group (28% vs. 15%, p = 0.47) (Figure-1). In the facial group, most patients were admitted between October and April (85%) (p < 0.01), while those in the non-facial group were mostly admitted between April and August (72%) (p < 0.01).

In the facial group, the sites of infection included the forehead (n = 4), preorbital (n = 5), orbit (n = 1), and jaw and cheek (n = 10). In the non-facial group, the sites of infection included the trunk (n = 1), upper extremities (n = 5), and lower extremities (n = 19). Infections of the lower extremities were the most common (Table-2).

2. Blood examination and imaging

No significant differences were observed in blood examination findings between the groups. Eighteen patients (90%) in the facial group underwent radiography, CT, and MRI, whereas 11 (44%) in the non-facial group underwent radiography only (Table-3).

3. Bacteriological characteristics

Blood cultures were performed for 24 patients, and penicillin-sensitive *Streptococcus pneumoniae* was isolated from 1 patient who had orbital cellulitis complicated with sinusitis. Needle aspiration was performed on 6 patients in the facial group and 8 in the non-facial group, and pus cultures were performed for 14 patients. Methicillin-sensitive...
Staphylococcus aureus (MSSA) was isolated from 7 patients, S. pyogenes and coagulase-negative Staphylococci (CNS) from 2 patients, and no bacterial isolates were found in 3 patients (Table 4).

4. Treatment
Both groups received empirical therapy with intravenous antibiotics (Table 5). Sulbactam/ABPC at 60-150 mg/kg/day in divided
doses every 6 or 8 hrs was administered significantly more often to the facial group (n = 9) than to the non-facial group (n = 3) (p = 0.013). In addition to SBT/ABPC, intravenous antibiotics were administered at a standard dosage to all patients.

**Discussion**

This retrospective study aimed to distinguish the clinical manifestations and bacterial pathologies of facial and non-facial pediatric cellulitis. Our results suggest that no significant differences existed in clinical manifestations between the groups, whereas seasonal differences in admissions were noted.

McNamara et al. identified dermatitis as a risk factor for cellulitis of the lower extremities. In addition, Ellis et al. reported a 1.3-fold higher incidence of cellulitis in the summer than in the winter for inpatients and outpatients. Although our study was designed for inpatients only, similar results were obtained. The ages of patients at admission exhibited a bimodal distribution, with 20% of patients < 5 years old, 15% < 10 years old, and 22% > 15 years old, which was similar to the bimodal distribution in our study (56% of patients < 5 years old, 4% < 10 years old, and 28% ≥ 10 years old; Figure-1). Regarding the site of infection, Ellis et al. reported that the lower extremities were infected in approximately 40% of cases, similar to our results of the lower extremities being infected in 42% of subjects (Table-2).

The rate of the oral administration of antibiotics at preadmission was approximately 30% in our study (Table-1). However, 70-90% of cellulitis patients were treated in the outpatient department and, thus, bacterial cultures were not considered to be cost-effective or useful. In the present study, none of the patients received pneumococcal vaccinations because this study was conducted before regular vaccinations in Japan.

Radiography, CT, and MRI were the most likely to be performed because of suspected periorbital and orbital cellulitis, necrotizing fasciitis, gas gangrene, osteomyelitis, intraorbital abscess, and infiltration into the central nervous system. These modalities were considered to have been employed more frequently to differentiate orbital cellulitis in the facial group.

Periorbital and orbital cellulitis may develop from upper respiratory tract inflammation, sinusitis, and impetigo, and are occasionally complicated with bacteremia. The incidence of bacteremia was approximately 4% in the present study, albeit to only 1 patient probably because of antibiotics administration before admission. Wathen et al. found that blood culture results never revealed a clinically significant organism in children with cellulitis.

Although the most common cellulitis pathogens are *S. aureus* and *S. pyogenes*, *Haemophilus influenzae*, *Clostridium* spp., and other anaerobic bacteria may also cause the disease. In the present study, needle aspiration was performed on 14 patients (31%). The resulting pus cultures were negative for bacteria in 3 patients (21%) (Table-4). Culture results from needle aspiration were positive in 5–40% of patients, and the cultures from punch biopsy specimens were positive for pathogens in 20–30% of patients. The rate of the positive identification of various culture inspections in cellulitis was not high. The culture of pus collected using needle aspiration is considered to be useful for the identification of bacteria according to the Infectious Diseases Society of America (IDSA) guidelines, showing a positive identification rate of 75–80%.

The administration of oral antibiotics before admission was a likely reason for the lower positive rate. In previous studies, *S. aureus* and *Streptococcus* infections were the dominant pathogens. Swartz found that Gram-positive cocci were the causative bacteria in 79% of cases, similar to the present study. Infectious sites in the jaw and cheek accounted for half of the cases observed in the facial group, while the lower extremities were infected in approximately three-fourths of cases in the non-facial group.

We selected CEZ and SBT/ABPC as empirical antibiotics for *S. aureus* or *S. pyogenes*. Empirical treatments based on β-lactam agents are recommended for non-compromised patients. However, patients with suspected methicillin-resistant *S. aureus* (MRSA) need to be administered anti-MRSA agents such as vancomycin (VCM). It is prudent to re-evaluate patients after 24–48 hrs in order to verify a clinical response, with progression despite the administration of antibiotics indicating...
infection with resistant microbes or a deep or severe infection\textsuperscript{1).} MRSA infection accounts for approximately 60\% of cases of cellulitis\textsuperscript{13}, but no patients was found in our study. In addition, the SBT/ABPC for empirical antibiotics were more frequently selected for the facial group than the non-facial group (p = 0.013). Broad antibiotics (e.g., SBT/ABPC) were administered in our study, because periorbital and orbital cellulitis may lead to severe infection. In the non-facial group, CEZ, an empirical antibiotic, was administered to approximately 50\% of cases (Table-5). Regarding empirical treatments, the IDSA guidelines recommend first-generation cephalosporin or penicillinase-resistant semisynthetic penicillin for 7–10 days\textsuperscript{1).} In the present study, the median duration of administration was 6 days (5–7 days) in the facial group and 6 days (4–7 days) in the non-facial group. No patients exhibited any sequela. The factors influencing the duration of intravenous antibiotics were considered to be improvements in CRP and local symptoms.

In conclusion, the aim of the present study was to distinguish differences in clinical manifestations between facial and non-facial cases of pediatric cellulitis. Admission was more common in the winter and spring for patients in the facial group and the spring and summer for those in the non-facial group; however, minimal differences were noted in clinical manifestations between the two groups.

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Conflict of interest

There are no conflicts of interest to declare.

References

1) Stevens DL, Bisno AL, Chambers HF, \textit{et al}; Infectious Diseases Society of America: Practice guidelines for the diagnosis and management of skin and soft-tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis, 2014; 59: e10–52.
2) Dupuy A, Benchikhi H, Roujeau JC, \textit{et al}; Risk factors for erysipelas of the leg (cellulitis): case–control study. BMJ, 1999; 318: 1591–1594.
3) McNamara DR, Tleyjeh IM, Berbari EF, \textit{et al}; A predictive model of recurrent lower extremity cellulitis in a population–based cohort. Arch Intern Med, 2007; 167: 709–715.
4) McNamara DR, Tleyjeh IM, Berbari EF, \textit{et al}; Incidence of lower-extremity cellulitis: a population–based study in Olmsted county, Minnesota. Mayo Clin Proc, 2007; 82: 817–821.
5) Ellis Simonsen SM, van Orman ER, Hatch BE, \textit{et al}; Cellulitis incidence in a defined population. Epidemiol Infect, 2006; 134: 293–299.
6) Howe L, Jones NS; Guidelines for the management of periorbital cellulitis/abscess. Clin Otolaryngol, 2004; 29: 725–728.
7) Wathen D, Halloran DR; Blood culture associations in children with a diagnosis of cellulitis in the era of methicillin–resistant Staphylococcus aureus. Hosp Pediatr, 2013; 3: 103–107.
8) McKinley SH, Yen MT, Miller AM, Yen KG; Microbiology of pediatric orbital cellulitis. Am J Ophthalmol, 2007; 144: 497–501.
9) Hook EW 3rd, Hooton TM, Horton CA, Coyle MB, Ramsey PG, Turck M; Microbiologic evaluation of cutaneous cellulitis in adults. Arch Intern Med, 1986; 146: 295–297.
10) Duvanel T, Auckenthaler R, Rohner P, Harms M, Saurat JH; Quantitative cultures of biopsy specimens from cutaneous cellulitis. Arch Intern Med, 1989; 149: 293–296.
11) Lebre C, Girard–Pipau F, Roujeau JC, Revuz J, Siaig P, Chosidow O; Value of fine–needle aspiration in infectious cellulitis. Arch Dermatol, 1996; 132: 842–843.
12) Swartz MN; Clinical practice. Cellulitis. N Engl J Med, 2004; 350: 904–912.
13) Gunderson GL; Cellulitis: definition, etiology, and clinical features. Am J Med, 2011; 124: 1113–1122.