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The clinical characteristics and risk factors for necrotizing soft tissue infection in children

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ABSTRACT

Importance: Necrotizing soft tissue infection (NSTI) is a serious infectious disease. However, the early clinical manifestations and indicators of NSTI in children are still unclear.

Objective: The purpose of this study was to analyze the clinical characteristics and risk factors of NSTI in pediatric patients.

Methods: A total of 127 children with skin and soft tissue infection (SSTI) were treated at our hospital and divided into two groups: the NSTI group and the non-NSTI group, based on their discharge diagnosis from January 2011 to December 2022. Then, we collected and analyzed the clinical characteristics and risk factors of all patients, including sex and age, disease inducement, admission temperature, local skin manifestations, infection site, the presence of sepsis, bacterial culture, and laboratory indicators.

Results: In our study, there was a statistical difference in the age distribution and disease inducement between NSTI and non-NSTI groups. The occurrence of local skin manifestations (blisters/bullae and ecchymosis) and the presence of sepsis significantly increased in the NSTI group compared to the non-NSTI group. Additionally, only the platelet count on laboratory tests was statistically different between the NSTI and non-NSTI groups. Finally, the logistic regression analysis suggested that local skin manifestations such as blisters/bullae, and ecchymosis, as well as the presence of sepsis, were identified as risk factors for NSTI.

Interpretation: Children with SSTI and skin manifestations such as blisters/bullae, ecchymosis, and the presence of sepsis are at a higher risk of developing NSTI. These symptoms serve as useful indicators for early detection of NSTI.

KEYWORDS

Clinical characteristics, Risk factors, Necrotizing soft tissue infection, Skin and soft tissue infection

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INTRODUCTION

Skin and soft tissue infection (SSTI) is an inflammatory disease caused by bacteria invading the epidermis, dermis, and subcutaneous tissue. Its clinical manifestations are diverse, including folliculitis, furuncle, carbuncle, lymphangitis, acute cellulitis, and even necrotizing soft tissue infection (NSTI). NSTI, including cellulitis, necrotizing fasciitis (NF), and myositis, results in rapid tissue destruction, systemic intoxication, and high mortality. Compared to adults, the clinical incidence of NSTI in children is rare, with an annual incidence of 0.08 per 100 000 people.[1] Owing to the rarity of NSTI, the time for clinical diagnosis and intervention is often delayed. In the United States, there is a 10% increase in the prevalence of NSTI in hospital admissions.[2] A previous report recommended the use of the laboratory risk indicator for NF (LRINEC) score as a diagnostic tool to differentiate NF from other SSTI.[3] However, the early clinical manifestations and indicators of NSTI in children are still unclear. We aimed to assess the clinical characteristics and risk factors of NSTI in children by reviewing over 10 years of clinical data on SSTI at our hospital.

METHODS

Ethical approval

This study protocol was approved by the Ethics Committee of Beijing Children's Hospital, Capital Medical University, National Center for Children's Health (No. [2023]-E-044-R). The data are anonymous, and the requirement for informed consent was therefore waived.

Data collection

From January 2011 to December 2022, a total of 127 patients with SSTI were admitted to Beijing Children's Hospital, Capital Medical University, National Center for Children's Health. The inclusion criteria for SSTI are as follows: (a) the presence of symptoms such as redness, swelling, heat, and pain in the local soft tissues; (b) the availability of complete clinical data. The exclusion criteria were as follows: (a) poor compliance and non-cooperation with the treatment; (b) transfer halfway or automatic discharge. During hospitalization, 58 patients were diagnosed with NSTI through surgical exploration. Thus, we grouped all patients with SSTI into two groups: the NSTI group (58 cases) and the non-NSTI group (69 cases).

First, the clinical characteristics were collected from all patients, including sex and age. Other data collected included disease predisposing factors, admission temperature, local skin manifestations (blisters/bullae and ecchymosis), infection site, presence of sepsis, bacterial culture, and laboratory indicators such as white blood cell count (WBC), neutrophil count, hemoglobin (HGB) level, sodium level, glucose level, creatinine level, platelet count (PLT), prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen level (FIB). In our study, the lesion sites of patients were grouped into six categories, including head and neck, upper limbs, trunk, lower limbs, buttocks, and multi-position. Clinically, sepsis is highly suspected if the patient has a confirmed infection and exhibits the following symptoms such as chills, fever, heart rate > 90 times/min, respiratory rate > 20 times/min, arterial carbon dioxide pressure < 32 mmHg, and poor mental state. Finally, the commonly used method is the LRINEC score, which involves monitoring serum levels of C-reactive protein, WBC, HGB, sodium, creatinine, and glucose.[3] A necrotic soft tissue infection is suspected when a patient's LRINEC score is greater than 6 (Table S1).

Statistical analysis

Statistical analyses were performed using SPSS software version 22.0. $P < 0.05$ was considered statistically significant. The categorical variables were represented as numbers (n) and compared between different groups using either Pearson's chi-square test or Fisher's exact test. The continuous variables were expressed either as mean ± standard deviation or as median and interquartile ranges, and were compared using either Student's t-test or the Kruskal–Wallis test. Then, we conducted a logistic regression analysis to predict the risk factors for NSTI.

RESULTS

Admission information of SSTI patients

In our study (Table 1), the overall male-to-female ratio was 1.42:1, and it was 1.46:1 between the NSTI and non-NSTI groups, respectively. The median age of NSTI patients was 15 months, compared to non-NSTI patients who had a median age of 25 months. The mean admission temperatures of the NSTI and non-NSTI groups were 38.90 and 38.69°C, respectively. There was no significant difference in sex and admission temperature between NSTI and non-NSTI groups, but a statistical difference in the age distribution of patients ($P = 0.005$). After analyzing the predisposing factors among all patients with SSTI, it was found that a significant number of cases had no identifiable predisposing cause such as rash/chickenpox, injection therapy, trauma/surgery, or immunodeficiency. Additionally, there was a statistically significant difference in the incidence of predisposing factors for SSTI between the NSTI and non-NSTI groups (Table 1, $P = 0.030$).

Infection information of SSTI patients

NSTI is an aggressive form of SSTI and can be caused by a wide variety of organisms, leading to severe

TABLE 1 The clinical characteristics of included children with skin and soft tissue infection

Variable	NSTI group ($n = 58$)	non-NSTI group ($n = 69$)	*P*
Sex			0.535
Male	34	41	
Female	24	28	
Age (months)	15 (9, 25)	25 (12, 44)	0.005
Maximum admission temperature (°C)	38.90 ± 0.81	38.69 ± 0.82	0.159
Predisposing factors			0.030
Not found	24	36	
Rash/chickenpox	16	16	
Injection therapy	7	3	
Trauma/surgery	5	13	
Immunodeficiency	6	1	
Local skin manifestations			
Blisters/bullae			<0.001
Yes	18	3	
No	40	66	
Ecchymosis			<0.001
Yes	33	8	
No	25	61	
Infection sites			0.059
Head and neck	1	8	
Upper limbs	6	10	
Trunk	6	3	
Lower limbs	27	34	
Buttocks	15	9	
Multi-position	3	5	
Presence of sepsis			<0.001
Yes	28	7	
No	30	62	
Bacterial culture			0.050
Gram-positive	27	38	
Gram-negative	18	6	
Laboratory indicators			
White blood cell ($\times 10^9$/L)	19.63 ± 12.57	20.04 ± 15.41	0.772
Neutrophil (%)	61.12 ± 18.68	59.26 ± 23.03	0.787
Hemoglobin (g/L)	103.60 ± 17.30	108.65 ± 14.74	0.104
Sodium (mmol/L)	132.52 ± 4.84	134.12 ± 3.51	0.074
Glucose (mmol/L)	5.39 ± 1.50	5.75 ± 2.23	0.510
Creatinine (μmol/L)	44.20 ± 39.78	31.82 ± 12.38	0.390
Platelet ($\times 10^9$/L)	277.70 ± 198.30	345.48 ± 166.45	0.012
Prothrombin time (s)	14.50 ± 5.23	13.65 ± 2.86	0.672
Activated partial thromboplastin time (s)	39.69 ± 12.69	36.71 ± 9.82	0.492
Fibrinogen (g/L)	3.84 ± 1.95	4.30 ± 1.60	0.050

Data are shown as *n* or mean ± standard deviation or median (interquartile range).
Abbreviation: NSTI, necrotizing soft tissue infection.

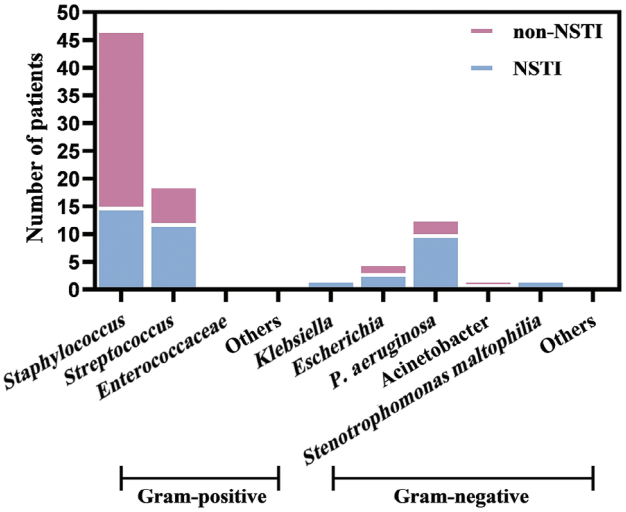

FIGURE 1 The specific classification of bacteria in children with skin and soft tissue infection. NSTI, necrotizing soft tissue infection.

infection of the skin, soft tissues, and muscles. The local skin manifestations, such as blisters/bullae and ecchymosis, were observed more frequently in the NSTI group compared to the non-NSTI group (Table 1, $P < 0.001$). The sites of infection were similar in both groups, with lower limbs being the most common site of infection in both groups. Sepsis was present in 48.3% of patients in the NSTI group, compared to 11.3% in the non-NSTI group ($P < 0.001$).

Next, we conducted bacterial cultures on the infection sites of patients during their hospitalization. Cultures were positive from infected sites in 79.3% of the NSTI group compared to 66.7% in the non-NSTI group ($P = 0.090$). The distribution of gram-positive and gram-negative bacteria was similar between the groups (Table 1, $P = 0.050$). The distribution of various bacteria in both groups is presented in Figure 1 and Table S2.

LRINEC scores of SSTI patients

According to the LRINEC score, the percentage of medium to high-risk patients increased in the NSTI group than in the non-NSTI group (43.10% *vs.* 31.88%, Table 2). Unfortunately, there were no statistically significant differences in the overall laboratory indicators (LRINEC scores) or in the individual laboratory indicators (WBC, neutrophil, HGB, sodium, lactate, creatinine, PT, APTT, and FIB) between the NSTI and non-NSTI groups, except for PLT (Table 1).

Treatment and prognosis of SSTI patients

Currently, empirical brood-spectrum antimicrobial treatment and early radical surgical debridement remain the key therapies in NSTI. First, all 127 patients immediately received empiric antibiotic therapy (cephalosporin, vancomycin, or meropenem), and antibiotics were adjusted after the results of bacterial culture were obtained. Then, the surgical debridement treatment was performed on 58 patients with NSTI as soon as possible. This treatment included direct excision, flap transplantation, skin grafting, negative pressure wound therapy, and other surgical techniques. Except for two patients who died due to sepsis, all NSTI patients were cured and discharged from our hospital. In the non-NSTI group, 40 cases underwent direct drainage or excision, six cases underwent negative pressure wound therapy, and others received only antibiotic treatment. Finally, all non-NSTI patients were cured and discharged from our hospital.

TABLE 2 The laboratory risk indicator for necrotizing fasciitis (LRINEC) scores in children with skin and soft tissue infection

Variable	NSTI group	non-NSTI group	*P*
LRINEC score	4 (3, 8)	4 (2, 6)	0.287
Low (<6)	33	47	
Medium (6–8)	8	8	
High (≥8)	17	14	

Data are shown as *n* or *n* (interquartile range).
Abbreviations: LRINEC, laboratory risk indicator for necrotizing fasciitis; NSTI, necrotizing soft tissue infection.

TABLE 3 The logistic regression analysis of risk factors for necrotizing soft tissue infection

Variable	B	OR (95% CI)	*P*
Age (months)	0.012	1.012 (0.994–1.030)	0.180
Predisposing factors	−0.314	0.730 (0.479–1.113)	0.144
Ecchymosis	−2.543	0.079 (0.022–0.283)	<0.001
Blisters/bullae	−2.373	0.093 (0.017–0.506)	0.006
Presence of sepsis	−1.346	0.026 (0.081–0.837)	0.024
Bacterial culture	0.512	1.668 (0.903–3.083)	0.102
Platelet ($\times 10^9$/L)	0.002	1.002 (0.999–1.004)	0.273

Abbreviations: CI, confidence interval; OR, odds ratio.

Analysis of risk factors for NSTI

Through the above analysis, significant differences were observed in age, predisposing factors, local skin manifestations (blisters/bullae and ecchymosis), the presence of sepsis, and the individual laboratory indicators (PLT). A logistic regression analysis was performed to understand the relationship between these factors and the patients' diagnosis of NSTI (Table 3). Logistic regression analysis suggested that local skin manifestations (blisters/bullae and ecchymosis), and the presence of sepsis were risk factors for NSTI.

DISCUSSION

NSTI is a type of severe infectious disease that causes progressive necrosis of the skin, subcutaneous tissue, fascia, and muscle.[4] Due to the rapid spread of pathogens along loose tissues, NSTI primarily occurs in the fascia, resulting in extensive tissue necrosis and potentially leading to sepsis or septic shock.[5] But it is difficult to distinguish whether the early soft tissue infection is necrotic.[6,7] Therefore, our aim was to analyze the clinical characteristics and risk factors of NSTI in children. In this study, we observed a statistical difference in the age distribution and predisposing factors between the NSTI and non-NSTI groups. The occurrence of local skin manifestations (blisters/bullae and ecchymosis) and sepsis significantly increased in the NSTI group compared to the non-NSTI group. Additionally, only the PLT on laboratory tests was statistically different between the NSTI and non-NSTI groups. Finally, logistic regression analysis suggested that local skin manifestations such as blisters/bullae, ecchymosis, as well as the presence of sepsis, were risk factors for NSTI.

Previous reports have shown that children, especially newborns, infants, and young adolescents, have a higher incidence of NSTI.[8] The possible reason is that younger children have a weaker skin barrier and looser subcutaneous tissue, making it easier for bacteria to invade the deeper layers of the skin, leading to infection and spread. Consistent with the references, the median age of patients with NSTI was younger than that of non-NSTI groups. In terms of predisposing factors for NSTI, malnutrition, low immunity, and preterm birth are more commonly observed in children compared to adults.[9] Some factors can make SSTI severe, including the patient's specific immunosuppression, locally rapidly progressing wound, surgical intervention, and so on.[10] However, no definite predisposing factors were found in nearly 50% of children with NSTI due to the limited sample size in this study. Therefore, in order to improve the detection of NSTI in children, it is important to recognize that some children may not have any previous trauma or underlying health conditions. However, the risk of mortality from this disease is higher in cases involving blunt trauma, general infection, chickenpox, and immunocompromised conditions.

At present, it is generally believed that early detection of clinical manifestations is beneficial in reducing the morbidity and mortality of NSTI in children. The main clinical manifestations of SSTI include soft tissue edema, erythema, severe pain, tenderness, fever, blistering, and bulbous or necrotic skin.[11] In the early stage of SSTI infection, severe local pain is the most important clinical clue, while ecchymosis and purple violet bullae on the skin surface are the typical signs of NSTI in the later stage.[10] For children, it is easier and more accurate to detect local blisters/bullae and ecchymosis than to assess the pain at the skin clinic. Our logistic regression analysis also suggested that local blisters/bullae and ecchymosis were risk factors for NSTI. Therefore, it is crucial to promptly perform local skin incision exploration when the aforementioned skin changes occur in children. Simultaneously, children with confirmed NSTI should undergo debridement surgery to prevent further deterioration of the condition.

Previous studies have reported that children, especially newborns and infants aged less than 1 year, are more likely to develop trunk NSTI than adults.[12] There were six children with trunk NSTI in this study, including two newborns and three infants aged less than 1 year. One possible explanation for this trend may be that the contact of urine and feces with the skin increases the vulnerability of children who wear diapers to skin infections and even soft tissue infections.[8] Of the different types of NSTI, NF in the extremities is the most common, followed by Fournier gangrene (NF of the perianal/genital region). There was no significant difference in the infected sites between the two groups, and the infections were primarily located in the lower limbs.

According to microbiology, NSTI is usually divided into NF type 1 (polymicrobial), NF type 2 (monomicrobial), Fournier's gangrene (polymicrobial), necrotizing myositis (*Streptococcus pyogenes*), and gas gangrene (*Clostridium spp*.).[1] In our bacterial culture results, the majority of our NSTI cases were classified as NF type 2. Furthermore, gram-positive bacteria were dominant in both groups. In the NSTI group, streptococcus accounted for 42.86% of the bacteria, while in the non-NSTI group, staphylococcus accounted for 80.00%. Therefore, we need to pay attention to the possibility of NSTI in patients when a streptococcal infection is detected in a wound bacterial culture of an SSTI in patients. In addition, there is growing concern about reports of drug-resistant bacteria. We found that drug-resistant bacteria were cultured in both groups.

The LRINEC scoring system, introduced in 2004, is used to diagnose NF. A critical score of 6 points indicates the presence of NF, while a score of less than 5 is considered low risk, a score of 6–7 indicates medium risk and a score of more than 8 indicates high risk. A previous study reported that the risk of NSTI was 75% when the LRINEC score was ≥ 8.[1] The LRINEC score has been shown to have a statistically significant correlation with the accurate diagnosis of NF and is a valuable clinical tool for determining NF diagnosis and guiding surgical management.[13] Our results showed that 17 out of 58 children with NSTI were at high risk, while 14 out of 69 children with non-NSTI were also at high risk. However, there was no significant difference in

LRINEC scores between the two groups, and the diagnostic value of LRINEC scores in children remains limited.

The presence of local skin manifestations and sepsis are risk factors for developing NSTI in young children with soft tissue infections. Our findings may assist clinicians in the early detection and treatment of NSTI in children.

CONFLICT OF INTEREST

None.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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