Necrotizing fasciitis in children in eastern Ontario: a case–control study

Tauyee Hsieh,[*] Lindy M. Samson,[†] Mona Jabbour,[†] Martin H. Osmond[†]

Abstract

Background: Early recognition and treatment are important factors that can help improve survival following necrotizing fasciitis. However, early recognition is complicated by the difficulty in distinguishing the infection from other, less serious soft-tissue infections such as cellulitis. We reviewed the charts of children presenting with necrotizing fasciitis at a tertiary care pediatric hospital in Ontario to document potential increases in the frequency of cases and to identify clinical and laboratory features that could help distinguish between necrotizing fasciitis and cellulitis.

Methods: Necrotizing fasciitis was defined as a soft-tissue infection characterized by necrosis of subcutaneous tissue and confirmed at surgery or on pathological examination. A retrospective chart review was conducted to identify cases of necrotizing fasciitis that occurred between June 1, 1983, and May 31, 1999. The characteristics of the identified cases, their clinical manifestations and the laboratory features at presentation were compared with those of matched controls admitted to the hospital with cellulitis.

Results: In total, 8 cases of necrotizing fasciitis were identified during the study period. There were no cases from 1983 to 1987, 1 from 1988 to 1991, 1 from 1992 to 1995, and 6 cases from 1996 to 1999. Compared with the children who had cellulitis, those who had necrotizing fasciitis were more likely to present with a generalized erythematous rash (odds ratio [OR] 11.0; 95% confidence interval [CI] 1.5–81.6) and a toxic appearance (OR 23.0; 95% CI 2.0–262.5). They were also more likely than the children with cellulitis to have a history of fever (8/8 v. 10/24, $p = 0.004$), a higher temperature (mean 38.7°C v. 37.8°C, $p = 0.006$), a higher respiratory rate (mean 31.5 v. 25.4 breaths/min, $p = 0.02$) and a lower platelet count on presentation (mean 194.0 v. 299.3 × 10^9/L, $p = 0.03$).

Interpretation: On presentation, factors that may help distinguish necrotizing fasciitis from cellulitis include a generalized erythematous rash, toxic appearance, fever and low platelet count.

Necrotizing fasciitis is a rapidly progressive soft-tissue infection characterized by necrosis of subcutaneous tissue. The usual causative organisms are group A β-hemolytic *Streptococcus* and *Staphylococcus aureus*. Although rare, necrotizing fasciitis can cause severe illness and has a high mortality rate, reported to be from 24% to 58%.[1,2] Recent studies have shown an increase in the number of cases in Canada[1] and the United States[3,4] among both children and adults. Among children the infection has been associated with varicella infection.[4]

Necrotizing fasciitis commonly presents as a rapidly spreading area of erythema, swelling and considerable pain. Aggressive surgery and débridement are usually required in combination with antibiotic therapy to limit the spread of the infection. Studies have shown that the most important factors that can help improve survival are early recognition and treatment.[5,6] However, early recognition is complicated by the difficulty in distinguishing it from other, less serious soft-tissue infections such as cellulitis, which presents with similar findings of erythema, swelling and pain. The identification of the key differences in presentation be-

Research

Recherche

From *the Faculty of Medicine, Queen's University, Kingston, Ont.; and †the Department of Pediatrics, University of Ottawa, Ottawa, Ont.

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tween necrotizing fasciitis and cellulitis is essential for early and effective management.

The objectives of our study were to document potential increases in the frequency of necrotizing fasciitis at a tertiary care pediatric hospital in Ontario, and to attempt to determine the unique clinical and laboratory features that distinguish necrotizing fasciitis from that of cellulitis.

Methods

We conducted a retrospective case–control study of all children with necrotizing fasciitis presenting to the Children's Hospital of Eastern Ontario (CHEO), in Ottawa. CHEO is a tertiary care hospital and the only pediatric inpatient facility in the city. Serving eastern Ontario and western Quebec, it has a catchment area of 1.5 million people and receives about 49 000 patient visits per year through the emergency department. The study design was approved by the CHEO Research Ethics Committee.

The charts of all children with necrotizing fasciitis under 18 years of age admitted to CHEO between June 1, 1983, and May 31, 1999, were reviewed. Necrotizing fasciitis was defined as a soft-tissue infection characterized by necrosis of subcutaneous tissue and confirmed at surgery or on pathological examination.[7] Cases were identified by searching the hospital's discharge diagnosis database using the International Classification of Diseases, 9th revision (ICD-9) code corresponding to the diagnosis of necrotizing fasciitis. To ensure that no cases were missed, all charts identified with the ICD-9 codes for myositis, gangrene, gas gangrene and erysipelas were also reviewed. Charts of children with group A β-hemolytic *Streptococcus* cultured from sterile sites during the same study period were also reviewed.

Control subjects were children under 18 years of age admitted and treated at CHEO for cellulitis. They were identified by ICD-9 codes based on the discharge diagnosis recorded by the attending physician. Control subjects were randomly selected and matched to the case subjects first by date of admission and then by closest date of birth (first by day, then by month and, if necessary, by year). Three control subjects were identified for every case subject.

To improve accuracy and to minimize inconsistencies in the review of the charts, a standard data abstraction sheet was used and the same person (T.H.) was responsible for extracting all the data. Age, sex, demographic information, diagnosis, site of infection, presenting signs and symptoms, comorbidities, blood values, culture results, treatment and outcome were recorded. Presenting signs and symptoms included focal swelling, focal erythema, focal pain, focal splinting, significant tenderness, generalized erythematous rash and "toxic appearance," as described by the emergency physician. If no record was made of these features they were assumed to be absent. Focal splinting was defined as refusal to use the affected part of the body. Significant tenderness was defined as substantial pain, as recorded on examination by the physician. Blood values obtained at presentation included the following: hemoglobin, white blood cell count and differential, platelet count, erythrocyte sedimentation rate, alanine aminotransferase (ALT) level and creatinine kinase level. Outcome fell into 1 of 4 categories: complete recovery, temporary disability requiring rehabilitation or further follow-up, permanent disability, or death.

A sample of charts (every case subject and 1 randomly selected control subject for each case) were reviewed independently in a blinded fashion by 3 of us (L.M.S., M.J., M.H.O.) to ensure that they met the case and control definitions and to monitor the performance of the chart abstractor. We met weekly during the study to resolve any disputes and maintain consistency in the selection and review of charts.

The data were analysed using Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. All significant risk factors were included in a multivariate analysis. Logistic regression analysis was used to derive the odds ratio for necrotizing fasciitis among patients with and without certain predisposing factors (e.g., toxic appearance, generalized erythematous rash). With 8 cases and 24 matched control subjects, the odds ratios could not be obtained from conditional logistic regression; however, we verified each estimate using a logit estimate of the odds ratio, adjusting for matching.

Results

The database search of ICD-9 codes corresponding to necrotizing fasciitis identified 12 patients, of whom 8 had infection that met the case definition; necrosis was not confirmed in the remaining 4 patients, and they were excluded from the study. We identified 145 patients with myositis, gangrene, gas gangrene or erysipelas; none had infection that fit the definition for necrotizing fasciitis. The review of a further 60 charts of patients with group A β-hemolytic *Streptococcus* cultured from a sterile site did not yield additional cases of necrotizing fasciitis.

Of the 8 cases of necrotizing fasciitis identified, none occurred between June 1, 1983, and May 31, 1987, 1 occurred between June 1, 1987, and May 31, 1991, another case occurred between June 1, 1991, and May 31, 1995, and 6 occurred between June 1, 1995, and May 31, 1999.

Of the children with necrotizing fasciitis, 3 were boys. The mean age was 5 years (range 2–13 years). Three cases occurred in winter, 3 in spring and 2 in fall. The case and control subjects did not differ significantly in terms of age and sex (Table 1).

Compared with the children who had cellulitis, those with necrotizing fasciitis were more likely to have a generalized erythematous rash (odds ratio [OR] 11.0, 95% confidence interval [CI] 1.5–81.6) and toxic appearance (OR 23.0, 95% CI 2.0–262.5). They were also significantly more likely to have a history of fever (8/8 v. 10/24, p = 0.004), a higher temperature (mean 38.7°C v. 37.8°C, p = 0.006), a higher respiratory rate (mean 31.5 v. 25.4 breaths/min, p = 0.02) and a lower platelet count on presentation (mean 194.0 v. 299.3 $\times$ 10^9/L, p = 0.03). The case subjects were more likely than the control subjects to have a lower diastolic blood pressure and a high white blood cell count ($> 15.5 \times 10^9$/L), although these differences were not statistically significant (Table 1). Similarly, although more case than control subjects had focal pain and focal splinting, these differences did not reach statistical significance. The 2 groups did not differ in terms of focal swelling, focal erythema, prior varicella infection, surgery or trauma.

Group A β-hemolytic *Streptococcus* was isolated in 7 and *S. aureus* in 1 of the children with necrotizing fasciitis. Of the children with cellulitis, group A β-hemolytic *Streptococ-*

cus was isolated in 4 patients and *S. aureus* in 5. Organisms identified in the patients with cellulitis were mainly isolated from the skin or eye. The cases of necrotizing fasciitis were more likely than those of cellulitis to be bacteremic (3/7 v. 1/23, p = 0.04) and to have group A β-hemolytic *Streptococcus* identified as the causative organism (7/8 v. 4/24, $p < 0.001$).

Interpretation

We found an increase in the number of cases of necrotizing fasciitis at CHEO over the past 16 years. This is consistent with findings from other studies.[1,3,4] In Ontario the incidence of invasive group A streptococcal infections, including necrotizing fasciitis, appears to be increasing, but numbers reported have varied from only 1 case in 1987 to 0.3 cases per 100 000 population in 1991[1] to 1.5 per 100 000 population in 1993.[8] In another Ontario study the incidence of group A streptococcal necrotizing fasciitis has been reported to increase from 0.085 per 100 000 population in 1992 to 0.4 per 100 000 population in 1994.[9] Our study showed an increase in the absolute number of cases, with a large increase in the last 4 years. Given that CHEO is the only pediatric inpatient facility in the Ottawa region, we believe that these numbers reflect a true increase in the number of cases of necrotizing fasciitis in our referral area.

Results from our study are consistent with the findings from a previous report[10] and suggest that the presence of a generalized erythematous rash and a toxic appearance are more predictive of necrotizing fasciitis than of cellulitis. Given that "toxic appearance" is a subjective description of a patient's overall clinical state, it may be difficult to incorporate such a parameter into a reliable clinical tool for diagnostic purposes. All of the children with necrotizing fasciitis had a history of fever. These patients were also more likely than the children with cellulitis to have a higher temperature, a higher respiratory rate and a lower platelet count. Thrombocytopenia was present in only 25% of the necrotizing fasciitis patients, but it was very specific in differentiating necrotizing fasciitis from cellulitis. Other studies have found focal pain and splinting to be important;[6,7] how-

Table 1: Demographic characteristics and clinical features at presentation of children with necrotizing fasciitis (case subjects) and those with cellulitis (control subjects) in eastern Ontario

Variable	Case subjects *n = 8*	Control subjects *n = 24*	*p* value
Mean age (and range), yr	5.00 (2.10–13.08)	4.62 (0.44–14.6)	0.69
Male sex, no. of children	3	16	0.22
Signs and symptoms, no. of children			
Generalized erythematous rash	4	2	0.02
Toxic appearance	4	1	< 0.001
Focal swelling	7	17	0.64
Focal erythema	7	24	0.25
Focal pain	7	7	0.10
Focal splinting	3	3	0.15
Significant tenderness	3	3	0.15
Vital signs			
Mean heart rate (and range), beats/min	136.25 (80–156)	121.42 (80–186)	0.10
Mean respiratory rate (and range), breaths/min	31.50 (20–48)	25.42 (18–38)	0.02
Mean systolic blood pressure (and range), mm Hg	104.88 (90–120)	*n = 19* 106.47 (86–130)	0.79
Mean diastolic blood pressure (and range), mm Hg	55.63 (40–80)	*n = 19* 64.53 (47–93)	0.07
Mean temperature (and range), °C	38.7 (38.0–39.4)	37.8 (36.1–40.7)	0.006
No. with history of fever	8	10	0.004
Blood values			
Mean white blood cell count (WBC) (and range), x 10^9/L	17.12 (3.14–40.5)	13.22 (5.64–23.5)	0.53
No. with high WBC*	5	6	0.09
No. with low WBC†	2	0	0.06
Mean hemoglobin level (and range), g/L	117.63 (95–141)	121.33 (101–143)	0.47
Mean platelet count (and range), x 10^9/L	194.00 (15–375)	299.33 (157–458)	0.03
No. with low platelet count‡	2	0	0.06
Comorbidity			
Varicella infection	4	7	0.40
Surgery	1	1	0.44
Trauma	2	12	0.41
Culture result, no. of children			
Group A β-hemolytic *Streptococcus*	7	4	< 0.001
Staphylococcus aureus	1	5	1
	n = 7	*n = 23*	
Positive blood culture	3	1	0.04
Outcome			
No. admitted to ICU	7	0	
Mean length of stay in ICU (and range), d	4.38 (0–11)	0 (0–0)	< 0.001
Mean total length of stay (and range), d	23.38 (17–38)	3.92 (1–14)	< 0.001
No. with temporary disability	7	2	< 0.001

Note: ICU = intensive care unit.
*High WBC = > 15.5 x 10^9/L.
†Low WBC = < 5.5 x 10^9/L.
‡Low platelet = < 150 x 10^9/L.

ever, these features, although more common in the children with necrotizing fasciitis than in those with cellulitis, did not differ statistically significantly between the 2 groups.

An increasing number of studies have identified invasive group A streptococcal infection, including necrotizing fasciitis, as a serious complication of varicella infection.[6,7,11–17] Although we found no statistically significant difference between the case and control subjects in the number of children with concurrent varicella infection, this comorbid condition was present in 50% and 27% of the subjects respectively. Thus, it would seem prudent to consider necrotizing fasciitis in children with varicella infection who have a secondary skin infection and a toxic appearance.

Given the retrospective nature of our study, it was limited because of missing data in some of the charts and a lack of standardization in the parameters reviewed. Because of the small number of cases of necrotizing fasciitis identified, potentially significant features may not have been identified.

In summary, we found that the number of cases of necrotizing fasciitis has increased over the past 16 years in the Ottawa region. Factors that help distinguish necrotizing fasciitis from cellulitis include a generalized erythematous rash, toxic appearance, fever and low platelet count. Further research of this disease and its presenting signs and symptoms, perhaps in the form of a large multicentre study, are needed to help clinicians with the early identification and treatment of these cases.

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Reprint requests to: *Dr. Martin H. Osmond, Division of Emergency Medicine, Department of Pediatrics, Children's Hospital of Eastern Ontario, 401 Smyth Rd., Ottawa ON K1H 8L1; fax 613 738-4852; osmond@cheo.on.ca*