

Necrotizing fasciitis secondary to chickenpox infection in children

Peter Clark, MD; Darin Davidson; Mervyn Letts, MD; Lou Lawton, MD; Ayman Jawadi, MD

Background: Necrotizing fasciitis is an uncommon but serious complication of chickenpox infection in young children. Because many of these infections affect the musculoskeletal tissues, orthopedic surgeons are often the first caregivers to be involved in diagnosis and treatment. Our objective was to review the diagnostic features of necrotizing fasciitis and analyze treatment methods to control and eradicate the musculoskeletal infection. **Design:** A review. **Setting:** The Children's Hospital of Eastern Ontario, Ottawa, a major Canadian pediatric trauma and referral centre. **Patients:** Five children who presented with necrotizing fasciitis secondary to chickenpox infection. **Intervention:** Surgical débridement of the involved area of necrotizing fasciitis and intravenous antibiotic treatment with clindamycin and penicillin. **Main outcome measures:** Complications and outcome. **Results:** The average age of the 5 children at presentation was 3.8 years (range from 2.9–5.8 yr). The necrotizing fasciitis involved the lower extremity in 5 children, the upper extremity in 3, and the abdomen, chest, neck and back in 1 child each. One child presented with involvement of all 4 extremities. In 4 children, culture specimens grew group A β -hemolytic *Streptococcus*. They all survived and all limbs were salvaged, although secondary closure and skin grafting were required. At an average follow-up of 1 year, each child had fully recovered with no loss of muscle function. **Conclusions:** Necrotizing fasciitis should be suspected in any child with a history of varicella infection and an increasing complaint of pain and swelling in an extremity or other body area associated with increasing fever, erythema, lethargy and irritability. Emergent surgical débridement and intensive antibiotic therapy are essential to prevent muscle necrosis, major limb dysfunction and death.

Contexte : La fasciite nécrosante est une complication rare mais grave de la varicelle chez les jeunes enfants. Comme beaucoup de ces infections atteignent les tissus musculosquelettiques, les chirurgiens orthopédiques sont souvent les premiers soignants à intervenir dans le diagnostic et le traitement. L'étude visait à revoir les caractéristiques diagnostiques de la fasciite nécrosante et à analyser des méthodes de traitement pour lutter contre l'infection musculosquelettique et l'éliminer. **Conception :** Étude. **Contexte :** Hôpital pour enfants de l'est de l'Ontario, Ottawa, grand centre canadien de référence et de traumatologie pédiatrique. **Patients :** Cinq enfants qui se sont présentés avec une fasciite nécrosante secondaire à une varicelle. **Intervention :** Débridement chirurgical de la zone touchée par la fasciite nécrosante et antibiothérapie intraveineuse à la clindamycine et à la pénicilline. **Principales mesures de résultats :** Complications et issue de l'intervention. **Résultats :** Les cinq enfants avaient en moyenne 3,8 ans (intervalle de 2,9 à 5,8 ans) lorsqu'ils se sont présentés. La fasciite nécrosante atteignait les membres inférieurs chez les cinq enfants, les membres supérieurs chez trois d'entre eux et l'abdomen, le thorax, le cou et le dos chez un enfant dans chaque cas. Dans un cas, les quatre membres de l'enfant étaient atteints. Chez quatre enfants, les spécimens de culture ont produit du streptocoque bêta-hémolytique du groupe A. Tous les enfants ont survécu et l'on a sauvé tous les membres atteints, même si des fermetures secondaires et des greffes de peau ont été nécessaires. Au suivi moyen à un an, chaque enfant s'était rétabli et n'avait perdu aucune fonction musculaire. **Conclusions :** Il faut soupçonner une fasciite nécrosante chez tout enfant ayant des antécédents de varicelle et se plaignant de douleur croissante et d'enflure d'un membre ou d'une autre région du corps associées à de la fièvre, à de l'érythème, à la léthargie et à l'irritabilité. Le débridement chirurgical d'urgence et une antibiothérapie intensive sont essentiels pour prévenir la nécrose musculaire, une dysfonction importante du membre et la mort.

From the Division of Orthopaedics, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Ont.

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Correspondence to: Dr. Mervyn Letts, Department of Surgery, Children's Hospital of Eastern Ontario, 401 Smyth Rd., Ottawa ON K1H 8L1; fax 416 738-4840

Chickenpox, caused by the varicella-zoster virus, is an extraordinarily contagious childhood illness. There are approximately 350 000 cases annually in Canada. Stokes¹ first documented soft-tissue complications of varicella in 1807,² and Hutchinson reported additional cases in 1882.³ Choo and associates⁴ estimated an overall complication rate of 2.1%. Recently, an increased incidence of serious complications has been noted. Peterson and colleagues⁵ found that 45% of complications involved soft-tissue infections, 18% involved the central nervous system (most notably encephalitis and cerebral ataxia), 14% involved the respiratory system and 10% the gastrointestinal system; 2% were bone or joint infections. Schreck and colleagues⁶ reported that 6% of all varicella complications were musculoskeletal.

Concomitant bacterial infection is common among the complications reported in previously healthy children with chickenpox. Group A β -hemolytic *Streptococcus* (GABHS) and *Staphylococcus aureus* are the major causative organisms.⁷ GABHS manifests as a deep-seated infection and is often the most severe and difficult to treat. Deep-seated infections are associated with thrombocytopenia, bacteremia, persistent fever, prolonged hospitalization requiring intensive care management, and the potential for a fatal outcome.^{7,8} In several cases affected children pre-

sented in septic shock.^{9,10} Peterson and associates¹⁰ described 25 cases of invasive infection in children with chickenpox, Zerr and colleagues¹¹ reported 19 cases of necrotizing fasciitis, and Mills and colleagues¹² reported 4 such cases. Other reported musculoskeletal complications include multifocal septic arthritis, pyomyositis and necrotizing pyomyositis.¹² The frequency of such complications appears to be increasing.¹³ Cowan and associates⁹ reported a series of invasive GABHS infections in 6 children with chickenpox over a 3-month period. In a study recently reported from our institution, 8 cases of necrotizing fasciitis were encountered over 12 months; of these, 4 occurred in children with chickenpox.¹⁴

To our knowledge, no studies of necrotizing fasciitis in children with chickenpox have been reported in Canada. Because of the increasing severity of complications in previously healthy children with varicella infections, we chose to review our experience regarding the incidence, type and management of such complications for the benefit of surgeons, who may be the first health care personnel to encounter the complication.

Patients and method

We reviewed the clinical, radiologic and operative records of all children admitted to our centre with necrotizing fasciitis and chickenpox

since January 1995. Cases were identified through a computerized search of hospital records. The English medical literature was thoroughly searched for reports of necrotizing fasciitis in children with chickenpox so that a comparison between previously encountered cases and the children in this series could be made.

Results

The series comprised 5 children (3 boys, 2 girls). The average age at presentation was 3.8 years (range from 2.9–5.8 yr) (Table 1). The medical history was unremarkable in each child. The average time from the onset of chickenpox vesicles to presentation with profound systemic symptoms was 5.2 days (range from 1–7d). The average duration of the presenting complaints and symptoms was 2 days (range from 1–4 d). The most common presenting complaints were pain and erythema (Table 2).

On clinical examination, the affected limb had a mottled erythematous appearance that increased in scope and intensity over the short period (2–4 h) of observation. Each child was tachycardic and tachypneic, 4 were febrile, and 2 presented with septic shock (Table 3). Laboratory findings included an elevated leukocyte count in 3 children, prothrombin and partial thromboplastin times in 3 and erythrocyte sedimentation rate in 2, and a decreased hemoglo-

Table 1

Cases of Necrotizing Fasciitis In Children With Chickenpox Seen at the Children's Hospital of Eastern Ontario Between 1995 and 2001

Case	Sex/age, yr	Elapsed time, d*	Site affected	Infecting organism	Associated conditions	Complications
1	F/3.25	6	Right thigh, abdomen	GABHS	None	Asymptomatic urinary tract infection
2	M/5.8	7	Left arm	GABHS	None	None
3	F/3.17	1	Left thigh	GABHS	Septic arthritis, osteomyelitis, septic shock	Compartment syndrome
4	M/4.0	7	All limbs	GABHS	Septic shock	Compartment syndrome; equinus contracture of right ankle, flexion contracture of fingers, flexion contracture of right knee
5	M/2.9	5	Chest, neck, back, shoulder	None	None	Scar hypertrophy

*Time from appearance of vesicles to development of necrotizing fasciitis
GABHS = group A β -hemolytic *Streptococcus*.

bin level in 3. The most commonly affected sites were the lower extremity in 5 children and the upper extremity in 3; 1 child presented with involvement of all 4 limbs (Table 1). Magnetic resonance imaging (MRI), performed in 4 children, was diagnostic in each case (Fig. 1). A presumptive diagnosis of cellulitis was made in 2 children with a subsequent diagnosis of necrotizing fasciitis, which was made on the basis of MRI and intraoperative findings. Associated complications included septic shock in 2 children, osteomyelitis of the distal femur with septic arthritis of the knee in 1 child and compartment syndrome another. There were no pulmonary or intra-abdominal complications. Cultures of tissue and blood grew GABHS, susceptible to clindamycin, penicillin, erythromycin and vancomycin in 4 of the children.

Table 2

Frequency of Presenting Complaints in 5 Children Having Necrotizing Fasciitis Associated With Chickenpox

Complaint	No. of children
Pain of affected site	5
Fever	4
Erythema	4
Lethargy	3
Nausea/vomiting	2
Irritability	2
Swelling of affected site	2
Erythema	1
Diarrhea	1

Table 3

Clinical Findings in 5 Children Having Necrotizing Fasciitis Associated With Chickenpox

Finding	No. of children
Tachycardia	5
Increased respiratory rate	5
Febrile	4
Tenderness of affected site	2
Hypotension	1
Cyanosis	1
Drainage from pustule	1

Treatment consisted of emergent surgical débridement in each child (Fig. 2). The average number of repeat débridements was 3.2 (range from 1–6). Three children received split-thickness skin grafts to the affected area. Immediate complications included asymptomatic urinary tract infection in 1 child (case 1) and compartment syndrome in 1 child (case 3). Additional procedures included fasciotomy in 2 children with compartment syndrome (cases 3 and 4) and drilling and fenestration in 1 child (case 3) with osteomyelitis. Each child was given antibiotics intravenously. All received clindamycin and 4 received penicillin. The average duration of intravenous administration was 15.8 days (range from 10–23 d). Adjunctive therapy consisted of acyclovir in 1 child (case 1) and human immune globulin in 1 (case 2). Four children were admitted to the intensive care unit; on average they stayed there for 6.5 days (range from 4–11 d). Delayed complications included equinus deformity of the ankle, flexion contractures of the

fingers, a knee flexion contracture in 1 child (case 4) and scar hypertrophy in another (case 5). The average overall duration of hospital stay was 20 days (range from 10–31 d). Two children were discharged on penicillin, 1 requiring intravenous administration via a Broviac catheter. The average length of follow-up was 1 year (range from 4 wk–2.25 yr). At the time of the most recent follow-up, each child had made a full recovery and had no sequelae.

Discussion

Bacteriologic findings in this series were similar to those previously reported (Table 4^{6,11,12,15–18}). Culture specimens in 80% of cases grew GABHS. Schreck and colleagues⁶ reported GABHS in 80%, and Aebi and associates⁷ found GABHS in 59% of cases and *S. aureus* in 28% of their series of 84 children with invasive infections. Brogan and associates¹⁵ reported on 14 children with necrotizing fasciitis secondary to varicella infection, in which

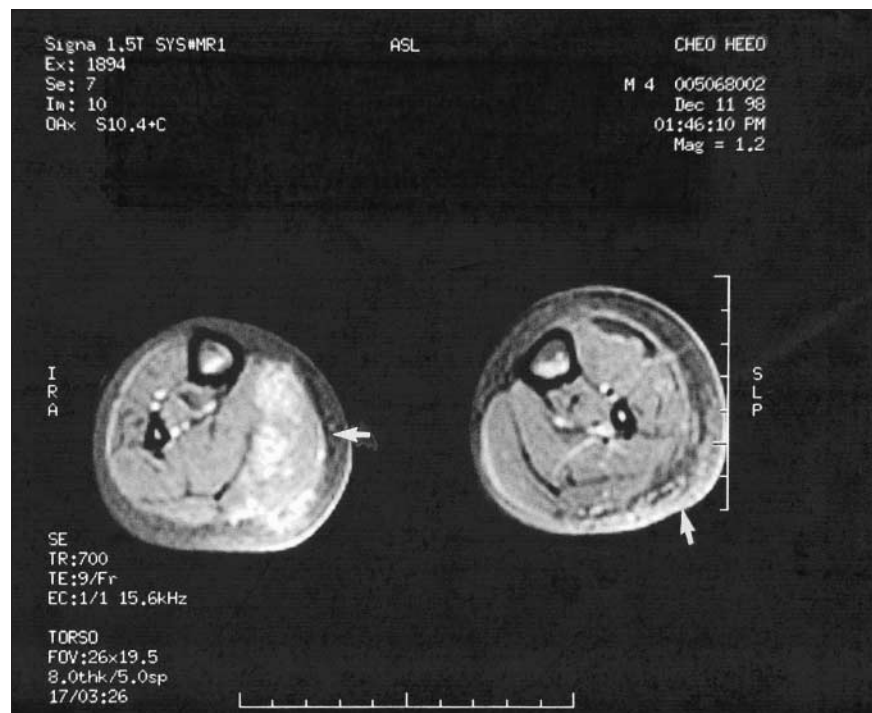


FIG. 1. Magnetic resonance image showing the typical appearance of necrotizing fasciitis (arrows) affecting both lower extremities in a 4-year-old boy (case 4). Diffuse muscle infiltration can be seen.

GABHS was the infecting organism.

A number of authors have described associated complications. Schreck and colleagues⁶ reported 2 cases of osteomyelitis, 2 of septic arthritis and 1 abscess. Grier and Feinstein¹⁹ also reported cases of osteomyelitis in children with chickenpox. In their study, there was 1 case of osteomyelitis of the distal femur with septic arthritis of the knee and 2 cases of compartment syndrome, all associated with the necrotizing fasciitis. The children with compartment syndrome had no permanent sequelae.

chickenpox is a ubiquitous infectious disease affecting over 60% of children. In most cases, it is only a mild irritant. Serious complications such as necrotizing fasciitis constitute less than 1% of cases.

Complications secondary to chickenpox infection have been reported to occur in younger children. The average age at the time of presentation in our study was 3.8 years, similar to the 3.1 years reported by Peterson and colleagues.⁵ Brogan and associates¹⁵ reported an average age of 4 years, and Waldhausen and

colleagues¹⁷ 4.5 years. Similarly, the average age of 19 children reported by Zerr and colleagues¹¹ was 4.6 years with the oldest child being 9 years of age. The average age of 5 children in a series reported by Schreck and colleagues⁶ was 2 years. Falcone and associates¹⁶ described the case of an 8-year-old girl. Vugia and colleagues¹⁸ reported a series of 24 children with chickenpox who suffered invasive infections; of these only a 6-month-old boy had necrotizing fasciitis.

In our study, the complications first developed an average of 5.2 days after the appearance of vesicles compared with 3 days in the study of Brogan and associates¹⁵ and 4 days in the study of Waldhausen and colleagues.¹⁷ In their study of 6 children with invasive GABHS infections associated with chickenpox, Cowan and associates⁹ reported an average of 6.5 days between onset of vesicles and presentation with infection. According to Aebi and associates,⁷ 27% of children in their study had deep infection and shock, and the death rate was 3.6%.

Schreck and colleagues⁶ described 27 musculoskeletal complications seen in children with chickenpox over a 10-year period, of which 7 were associated with septic shock, and 3 of the 6 children in the study of Cowan and associates⁹ presented



FIG. 2. Appearance of affected tissue at the time of operative débridement.

Table 4

Reported Cases of Necrotizing Fasciitis In Children With Chickenpox*

Study	No. of cases	Average age, yr	Infecting organism	Complications
Schreck et al ⁶	5	2	GABHS 60%; <i>Staphylococcus aureus</i> / <i>Pseudomonas</i> 20%; none 20%	Bacteremia 1 (20%); septic shock 2 (40%)
Zerr et al ¹¹	19	4.4	GABHS 84%; other 10%; none 5%	Septic shock 5 (26%)
Mills et al ¹²	1	10	GABHS	None
Brogan et al ¹⁵	14	4	GABHS 100%	Sepsis 5 (36%)
Falcone et al ¹⁶	1	8	GABHS	Septic shock; respiratory deficiency
Waldhausen et al ¹⁷	18	4.5	GABHS 78%; <i>Staphylococcus aureus</i> 11%; none 11%	No mention
Vugia et al ¹⁸	1	0.5	GABHS	No mention
Current study	5	3.8	GABHS 80% negative 20%	Septic shock 2 (40%); urinary tract infection 1 (20%); compartment syndrome 2 (40%); scar hypertrophy 1 (20%); joint contracture 1 (20%)

*There were no deaths.
GABHS = group A β -hemolytic *Streptococcus*.

with septic shock. In our study, 2 of the 5 children presented with septic shock, and both had blood cultures that grew GABHS. None of our children died. Belani and associates²⁰ reported death rates secondary to bacteremia with GABHS between 7% and 35%, despite early antibiotic therapy. Waldhausen and colleagues¹⁷ advocated early operative treatment in these cases to prevent fatal complications. In our study all children successfully underwent early operative intervention and received antibiotics intravenously, and we recommend aggressive operative débridement.

The diagnosis of complications secondary to chickenpox in children may be difficult in the early stages of disease. Contributing factors are high, persisting fever, recurrent fever after afebrile periods, localized swelling, induration, erythema, disproportionate pain, pseudoparalysis, refusal to bear weight, lethargy or toxic appearance, hypotension and tachycardia. In a recent study, Hsieh and associates¹⁴ reported that necrotizing fasciitis can be distinguished from cellulitis on the basis of diffuse erythema, toxic appearance, fever and thrombocytopenia. Although some authors have advocated immediate surgical intervention,¹⁷ MRI can be helpful in localizing the site of infection and differentiating necrotizing fasciitis from cellulitis, septic arthritis and osteomyelitis, as well as in delineating the affected tissues, thereby assisting in surgical planning.²¹ Four children in our series underwent MRI preoperatively; the investigation was diagnostic in each case. It also allowed for more precise determination of the depth and extent of the infection. We recommend MRI for its value in helping to plan the extent of débridement required. In contrast, Mills and colleagues¹² noted that the use of imaging in a seriously ill child, although contributing to the diagnosis, may result in further morbidity secondary to a delay in definitive treatment. They, therefore, recommended emergent

surgical exploration with irrigation and débridement for any child with evidence of invasive infection. We carried out surgical débridement after MRI in 4 of the 5 children and encountered no complications due to the delay in surgery, which was no longer than 2 hours.

Several factors contribute to the pathogenesis of necrotizing fasciitis in children with chickenpox. The vesicle creates a full thickness dermal lesion that provides a route for bacteria to spread from the skin surface into the subcutaneous tissues.^{11,13} There are numerous virulence factors of GABHS. The M surface protein repels macrophages and complement. Streptococcal pyogenic exotoxins A, B and C initiate release of tumour necrosis factor- α and interleukin-1, resulting in fever, rash, direct toxic effects to the endothelium, septic shock and T-cell activation.¹⁵ Streptococcal M protein and exotoxins A and B have been reported in association with more severe infection.^{18,22} The organism also secretes hyaluronidase and streptolysin, allowing for tissue invasion and damage. Surgery is necessary to remove the necrotic tissue, the source of the exotoxins that are the cause of circulatory collapse, multiple organ failure, and eventually death.^{12,17}

Wilson and colleagues²³ reported that streptococcal pyogenic exotoxin B is cleaved to an active proteinase and is found in all isolates of GABHS necrotizing fasciitis. Antibodies to these proteins are likely important disease modifiers. Very young children, who have had little exposure to streptococcal infections, are therefore at higher risk for a deep infection because they are unlikely to possess antibodies to these proteins. The use of human immune globulin has resulted in clinical improvement by boosting the required antibodies.^{23,24} Human immune globulin was administered to only 1 child in this series; however, it did not seem to significantly affect the outcome, as the remaining 4 children also recovered fully. *Streptococcus*,

unlike *S. aureus*, is not usually resistant to penicillin, but when GABHS is present in large concentrations and reaching stationary growth, the bacteria exhibit decreased penicillin-binding-protein expression making it much less sensitive. For this reason, clindamycin is the drug of choice since it is not subject to the inoculum effect. Clindamycin was administered to each child in this series, with 4 children also receiving penicillin.

Peterson and associates¹⁰ reported several associations between invasive GABHS infection in children with varicella and children with varicella but no secondary infection. Associated factors included asthma, contraction of varicella-zoster virus from a household contact, fever persisting past the second day after appearance of the vesicles, and a delay in presentation for medical care. Zerr and colleagues¹¹ further reported an association between children using nonsteroidal anti-inflammatory drugs (NSAIDs) and the development of necrotizing fasciitis, who had more severe complications, including an increased risk of renal insufficiency and streptococcal toxic shock syndrome. No child in our series had a history of NSAID use.

The complications we have described are preventable with vaccination for chickenpox, which has been proved effective in preventing and decreasing the severity of infection.⁶ Numerous studies have advocated such vaccination to prevent infection and consequently to eliminate complications of chickenpox.^{6,18,23-27} This should be the standard of practice since the complications of chickenpox seem to be increasing in severity, with an increased frequency of GABHS infections. Current guidelines advocate vaccination for varicella in all children between 12 and 18 months of age and in children between 19 months and 12 years of age who have not previously been vaccinated or who have no history of varicella-zoster infection.²⁶ The vaccine has also been found to be effective in unvaccinated

children if it is given within 36 hours of exposure to chickenpox.²⁸ For children having varicella, acyclovir has been reported to decrease the severity and duration of infection, thereby decreasing the risk of complications.^{29,30} Acyclovir was administered to 1 child in our study.

In this series, delayed complications associated with the necrotizing fasciitis were encountered in 2 children. They included scar hypertrophy (case 5) and multiple joint contractures (case 4). Although these delayed complications may be the source of continued morbidity, previous studies have not described delayed complications. The child with scar hypertrophy required further surgical scar revisions. The other child required an ankle-foot orthosis to treat an equinus contracture of the ankle and continued follow-up for flexion contractures of the knee and fingers. Despite these complications, at the most recent follow-up the child was fully functional, had a normal gait, and had returned to all activities with no contractures.

Conclusions

Musculoskeletal complications of varicella infection affect children. In cases involving GABHS, these complications may be fatal. Early diagnosis and early surgical intervention are essential in successful management. Therefore, all primary caregivers and orthopedic surgeons must be aware of the potential for serious infection in cases of chickenpox and must treat any necrotizing fasciitis emergently. Initial antibiotic coverage should cover both GABHS and *S. aureus*; concurrent administration of acyclovir and human immune globulin can be included in the medical management. Vaccination against varicella infection should become the standard of care in order to prevent these serious complications.

Competing interests: None declared.

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