A Retrospective Review of Necrotizing Fasciitis in Thammasat University Hospital

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Objective: *Necrotizing fasciitis is a rapidly progressive soft tissue infection. Clinical features and microbial knowledge will help reduce mortality and morbidity from delayed diagnosis and treatment.*

Material and Method: *From January 2004 to December 2009, records of 222 necrotizing fasciitis patients were reviewed for the study. The following data were collected and recorded: age, sex, location of lesion, inciting event, clinical manifestation, culture and sensitivity and procedures.*

Results: *The male-to-female ratio was 1.4:1 with 56.3 years mean age. The most of the occupations were elderly who stay at home and laborers. The highest incidence rate was during the raining seasons. The most common infection site was at the lower extremity with unknown inciting event. A common underlying disease was diabetes. The major complains presented was skin lesion, fever with chill, conscious change, gastrointestinal symptom. Examination revealed erythematous and swelling skin lesion(100%), fever (50.9)%,hypotension blood pressure (32.4%). Positive wound culture isolation was 55.9% and in blood culture was 48%. Dominant gram negative bacteria (71.98%) were in wound culture but gram positive bacteria (51.28%) were dominant in blood culture. Polymicrobial isolates in wound culture was 48% and in blood culture was 6%. The average 2.5 procedures were debridement (33.8%), skin graft coverage (59.9%), amputation (15.4%). Mortality rate was 5.9% that 46.2% were diabetes.*

Conclusion: *Gram negative organisms were predominant wound isolates whereas gram positive organisms were predominant blood isolates. With high polymicrobial isolation, clinical manifestation can be described as necrotizing fasciitis type I. The elderly and diabetic patients were at risk. Early diagnosis is important in patients with fever, toxicity and erythematous swelling skin findings. The hallmarks of treatment are prompt surgical opening and debridement to get rid of the source of infection and broad-spectrum antibiotics treatment administered.*

Keywords: *Necrotizing fasciitis, Thammasat university hospital*

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Necrotizing fasciitis is a rapidly progressive soft tissue infection. Its progress is extremely fast, with extensive necrosis involving the skin, subcutaneous tissue, superficial fascia or may be muscle. Sepsis and toxemia lead to multiple organ failure and end up with abrupt and high mortality. Mortality rates can be almost 100% if early surgical intervention is not performed[1]. It is believed that necrotizing fasciitis can be caused by the synergistic of various aerobic or anaerobic, or gas producing, bacteria. But many literatures reported that monomicrobial infection is caused predominantly by *Streptococcus* group A. From his experiences in necrotizing fasciitis treatment, the author suspected that gram negative organism may be the predominant cause in this hospital.

This article reviews necrotizing fasciitis in Thammasat University Hospital. The clinical presentation, the microbiology, the treatment and results were the aids of reviews.

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Material and Method

From January 2004 to December 2009, the records of the patients who were diagnosed with necrotizing fasciitis and admitted in Thammasat University Hospital were reviewed.

Three hundreds and twenty seven patients were admitted but there were only records available for 222 patients.

The following data were collected: age, sex, location of lesion, inciting event, underlying disease,

clinical manifestation, culture and sensitivity and results

Results

General characteristics

There were 129 males and 93 female patients. Male-to-female ratio was 1.4:1. The mean age was 56.3 years (rang, 2-87 years). The mean age in males was 55.5 years. The mean age in females was 57.2 years.

Their occupations were mainly: unemployed and stayed at home (46%) and laborers (21.9%). Amongst those who stayed at home, the average age was 62.8 years (range, 32-87 years).

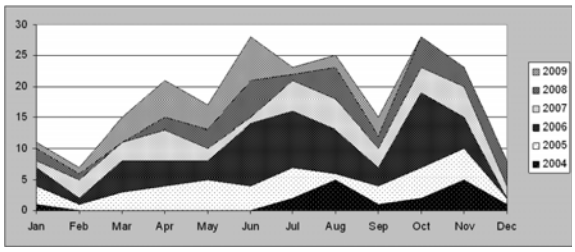

Fig. 1 Distribution of patients showed high incidence in June-August and October-November that were early and late raining season in Thailand

Table 1. Timing before admission (n = 222)

Day	Number	%
1	76	34.2
2	40	18.0
3	40	18.0
4	11	5.0
5	15	6.8
6	2	0.9
7	19	8.6
7-14	4	1.8
More than 14	15	6.8

Table 2. Infection site (n = 222)

Site	Number	%
Foot	93	41.9
Leg	109	49.1
Hand	9	4.1
Forearm	10	4.5
Arm	1	0.5

Timing of Incident, Location of lesion and Inciting event

The timing of incident was two high-peak periods, highest being June to August, the raining season in Thailand (Fig. 1). The time from onset to hospitalization averaged 5.04 days (range, 1-90 days) and hospitalization within 1, 3 and 7 day was 34.2%, 70.2 and 91.5%, respectively (Table 1).

Locations of the infection sites that were dignosed as first episode skin lesion, were: leg (49.1%), foot (41.9%), forearm (4.5%), hand (4.1%) and arm (0.5%) (Table 2).

Only eighty-eight cases (39.6%) had known inciting event. These included cuts or lacerations (17.1%), blunt trauma (7.7%), burns (4.5%), traffic injuries (3.6%), insect bites (3.6%) and abscesses (3.2%) (Table 3).

Underlying diseases were diabetes (53.7%), hypertension (37%), cirrhosis (9.8%), renal disease (6.3%), old cerebrovascular disease (4.4%), heart disease (8.3%) (Table 4).

Clinical manifestation

The major complain was skin lesion (43.7 %). The others were fever with chill (33.3%), conscious change (17.6%), gastrointestinal symptom (2.7%). (Table 5).

The vital signs: 50.9% had fever and 20.3%

Table 3. Inciting event (n = 222)

Cause	Number	%
Unidentified	134	60.4
Cut / laceration	38	17.1
Fall/contusion	17	7.7
Burn	10	4.5
Traffic	8	3.6
Animal bite	8	3.6
Abscess	7	3.2

Table 4. Patient underlying disease (n = 222)

Disease	Number	%
Diabetes	119	53.6
Hypertension	82	36.9
Cirrhosis	22	9.9
Heart disease	18	8.1
Renal disease	14	6.3
Celebrovascular	10	4.5

with fever more than 38 °C. The number of patients with hypotension blood pressure was 32.4%. All patients had erythematous and swelling skin lesion upon examination (Table 6).

Culture and sensitivity

The reports of wound and blood culture done on the day of admission were used. The wound culture was not done in two of 222 patients. All wound cultures were performed by deep infected tissue collection. Positive isolates report was found in 123 patients (55.9%). The number of isolation per specimen was as follows: single isolate -52%, double isolates -26%, three isolates -13%, four isolates -2.4% and more than four isolates -6.6%. The average number of isolations was 1.88 per patient (Table 7).

The common isolated organisms in the wound cultures were *Psuedomonas aeruginosa* (14.66%), *Escherichia coli* (12.07%), *Enterobacter* (11.64), *Klebsiella pneumoniae* (11.21%), *Acinetobacter baumannii* (9.91%), *Staphylococcus coagulase negative* (7.33%) (Table 8).

Sensitibility to antibiotic, *Psuedomonas aeruginosa* is sensitive to ceftazidime 70.6% (24/ 34), gentamicin 61.8% (21/34) *Escherichia coli* is sensitive to cefotaxine and gentamicin 60.7% (17/28), amikacin 89.3% (25/28).

Enterobacter spp. is sensitive to gentamicin 92.6% (25/27).

Klebsiella pneumoniae is sensitive to amoxycillin/clavulanic acid 80.8% (21/26), gentamicin 92.3% (24/26).

Staphylococcus coagulase negative is sensitive to amoxycillin/clavulanic acid and clindamycin 88.2% (15/17).

Blood cultures were done with 71 patients

Table 5. Main complain presentations (n = 222)

Main complain	Number	%
Skin lesion		
Inflammation	74	33.3
Discharge	14	6.3
Necrosis/bleb	9	4.1
Fever with chill	74	33.3
Conscious change	39	17.6
Gastrointestinal symptom	6	2.7
Low grade fever	4	1.8
Tachypnea	2	0.9

Table 6. Clinical examination presentations (n = 222)

Clinical examination	Number (n)	%
Temperature (°C)		
more than 37.5-38	68 (222)	30.6
38-40	44 (222)	19.8
more than 40	1 (222)	0.5
Blood pressure less than 90/60 mmHg	72 (222)	32.4
Erythematous and swelling skin lesion	222 (222)	100

Table 7. Number of isolated organism from wound culture (n = 123)

No. of organisms	Number	%
1	64	52
2	32	26
3	16	13
4	3	2.4
5	5	4.2
6	2	1.6
7	1	0.8

Table 8. Isolated organism from wound culture (n = 232)

Organism	Number	%
- Gram Negative	167	71.98
Pseudomonas aeruginosa	34	14.66
Escherichia coli	28	12.07
Enterobacter spp	27	11.64
Klebsiella pneumoniae	26	11.21
Acinetobacter baumannii	23	9.91
Proteus mirabilis	12	5.17
Proteus vulgaris	3	1.29
Citrobacter freundii	8	3.45
Citrobacter spp	2	0.86
Salmonella spp	3	1.29
Aeromonas spp	1	0.43
- Gram Positive	65	28.02
Staphylococcus, coagulase negative	17	7.33
Staphylococcus aureus	14	6.03
Streptococcus, gr. A beta-hemolytic	8	3.45
Streptococcus, gr. B beta-hemolytic	9	3.88
Streptococcus, gr. D-not Enterococci	6	2.59
Streptococcus, not gr. A, B and D	6	2.59
Streptococcus viridan	3	1.29
Streptococcus Agalactiae	2	0.86

(32%) and the number with positive isolated specimens was 34 (48%). The number of isolations per specimen was as follows: single isolate - 94% and double isolate - 6%. Average number of isolation was 1.29 per patient. (Table 9).

The common isolated organisms in blood culture were Staphylococcus, coagulase negative (41.67%), Psuedomonas aeruginosa (22.22%) (Table 10). Only 5 patients had similar organisms that was isolated in both wound and blood culture. They were *Psuedomonas aeruginosa*, *coagulase negative Staphylococci, Escherichia coli, Samonella spp* and *beta-hemolytic Streptococcus*. There was no difference between the gram negative and positive from the same isolated organisms (Table 11).

Sensitivity to antibiotic: Staphylococci coagulase negative was sensitive to amoxycillin/clavulanic acid 80.0% (12/15), clindamycin 86.7% (13/15), ciprofloxacin 93.3% (14/15).

Psuedomonas aeruginosa was sensitive to ceftazidime and cefoperazone/sulbbactam 87.5% (7/8), gentamicin 75% (6/8)

Treatment and results

All patients underwent urgent wound exploration for definite diagnosis and continued with opening debridement.

The number of cases with 1) only debridement was 33.8%. 2) Skin graft coverage was 59.9%. 3) Finger/toe amputation (9%), 4) Amputation done below knee (4.1%) and 5) above knee (2.3%) (Table 12).

Number of procedures averaged 2.5 (range: 13-1). Hospitalization days averaged 32.7 days (range: 1-166).

Mortality rate was 5.41% (12/222) of which 50% (6/12) was diabetic. There were different gram negative and positive isolates in the mortality review (Table 13, 14).

Discussion

Many different names have been used to describe such various necrotizing infections although they often have common pathology. In 1924 Meleney [2]noticed a necrotizing infections of skin and soft tissues caused by hemolytic *Streptococcus*.

Table 9. Number of isolated organism from blood culture (n = 34)

No. of organisms	Number	%
1	32	94
2	2	6

Table 10. Isolated organism from blood culture (n = 36)

Organism	Number	%
- Gram Negative	17	47.22
Pseudomonas aeruginosa	8	22.22
Escherichia coli	2	5.56
Klebsiella pneumoniae	2	5.56
Acinetobacter baumannii	2	5.56
Enterobacter spp	1	2.78
Salmonella spp	1	2.78
Shewannella pnterfacion	1	2.78
- Gram Positive	19	52.78
Staphylococcus , coagulase negative	15	41.67
Streptococcus, not gr. A,B and D	2	5.56
Staphylococcus aureus	1	2.78
Streptococcus viridan	1	2.78

Table 11. Similar isolated organism in both wound and blood culture

Organism	No.
Burkholderia (Pseudomonas) pseudomallel	1
Escherichia coli	1
Salmonella spp	1
Staphylococci, coagulase negative	1
Streptococci , beta -hemolytic not gr.A,B,D	1

Table12. Definitive operative treatment (n = 222)

Operation	Number	%
Skin graft	113	50.9
Debridement Only	75	33.8
Above Knee	5	2.3
Below Knee	9	4.1
Finger/toe amputation	20	9.0

Table 13. Discharge Status (n = 222)

Status	Number	%
Alive	204	91.89
Dead	12	5.41
Refer	6	2.70

Table 14. Mortality review (n = 12)

No.	Sex	Age	Site	Underlying disease	Wound culture	Blood culture
1	F	59	foot	chronic hepatitis	Not done	No growth
2	F	56	leg	diabetas	P. aeruginosa ,A. baumannii	Not done
3	M	41	leg	hypertension	No growth	Not done
4	M	60	leg	diabetes	Not done	Escherichia coli
5	F	67	leg	diabetes	Not done	Not done
6	F	72	leg	none	Staphylococcuse coagulase negativ	Not done
7	F	57	foot	SLE	No growth	No growth
8	M	49	leg	diabetes	No growth	No growth
9	F	70	leg	diabetes	Streptococcus gr A	Not done
10	M	37	foot	chronic hepatitis	A. baumanni, E. coli	Not done
11	F	74	foot	diabetes	Not done	No growth
12	F	76	leg	none	Not done	Streptococcus gr A

Wilson[3], in 1952, described accurately the most consistent features of the infection and first used the term of Necrotizing fasciitis. It is important because the diagnosis was based upon clinical features. Many medical and surgical literatures reviewed many different types of necrotizing infections because they may provide early clinical diagnosis clues and so surgical interventions are done early. Some literatures categorized necrotizing fasciitis into two main clinical types[4,6]:

Type I mixed infections that predominant may be gram positive or negative and aerobic and anaerobic; most common in patients with diabetes and peripheral vascular disease.

Type II monomicrobial, main organism may be *Streptococcus* group A (streptococcus toxic shock syndrome) or *Staphylococcus aureus* (staphylococcal toxic syndrome).

In this study, necrotizing fasciitis manifested in both male and female with almost equal ratio and mean age. The patients often were elderly who stay at home. The common underlying disease was diabetes. The incidence was high during the raining season that presents a suitable environment for bacterial growth. The most common infection site was the lower extremity and inciting event was often unknown because the lower extremity was prone to unconcern minor trauma or insect bite.

Clinical manifestation showed that even though the main complain was localized inflammation skin but upon examination all had localized erythematous and swelling skin lesions. In some patients, symptoms and signs of local inflammation were not initially apparent; this most likely occurred in elder or bed-ridden patients who often were diabetic. The absence of pain may be due to peripheral neuropathy.

Swelling and ill defined border erythema are usually present although it is not the main complain. Within 24-48 hours, they developed to a darkened to reddish-purple color with blisters or bullae or bleb (Fig. 2). Bullae can occurr in normal looking skin. The bullae are first filled with clear fluid and rapidly turn turbid. When the bullae are present, it means that there are already extensive skin destruction and severe compromised vascularization (Fig. 3). At this stage the patients will experience fever with chill due to presence of bacteria in the lymphatic system leading to systemic toxemia or bacteremia[5]. Subcutaneous crepitation is present in about 10 percent of the patients.[6] The time of onset before hospitalization was

Fig. 2 Bleb, sign of already necrosis of superficial fascia

early and may be the cause of rapid clinical deterioration.

Systemic manifestation, fever, malaise, myalgias, diarrhear and anoexia are often present in first 24 hours. Hypotensive blood pressure may occur initially or after but clinical sepsis always starts in the form of "warm shock"[7]. Often hypotensive shock and oliguria are not present but serum creatinine rises and results in renal failure.

Imaging for diagnosis were not reviewed in this study. CT scan or plain x-ray may help to detect if there is gas in soft tissue. MRI may not detect air along the fascial planes and cannot differentiate cellulitis from inflammation[8]. Ultrasound, Yen et al, was found to have a sensitivity of 88% and a specificity of 93%. Their criteria included diffuse thickening of the subcutaneous tissue accompanied by a fluid accumulation more than 4 mm in depth along the fascial layer, when compared to the normal limb[9]. In this reviews, clinical and wound exploration were major tools in diagnosis.

Because anaerobic cultures were not done in this hospital, only aerobic cultures were collected. Although the patients were usually on antibiotics before, positive isolation were high in both wound and blood culture. The sensitivity to commonly-use antibiotics was susceptibility. If the clinical conditions did not improved, it is beneficial for antibiotic adjustment with reference to the culture and sensitivity. This study shows that in the wound culture was gram negative bacteria predominantly (71.98%) whereas in blood culture it was gram positive bacteria (51.28%). Comparative to other countries[6,12] literatures suggest that Streptococcus group A or Staphylococcus aureus were the predominant group. But in correspondence to the other reviews in the north-eastern of Thailand, the predominant group in wound culture were gram negative bacteria and Pseudomonas aeruginosa[10].

There were no difference between gram negative and positive of the same isolated culture in both wound and blood. Wound cultures with more than one isolated organisms was 48% and in blood culture was 6%. Polymicrobial isolates were not predominant but just rather high. The synergistic of various bacterial causes should be considered and early broad-spectrum antibiotics treatments administered.

All patients were diagnosed early with necrotizing fasciitis and underwent urgent debridement and pre and post-operation intensive cares. Mortality rate was 5.9%, diabetes being one of the underlying factors.

In this review "Necrotizing fasciitis type I" was the predominant category as well as reported in some reviews in Thailand.

The mortality rate was rather low compared to many studies (11.7-21%)[6,10-12] but the morbidity rate was very high. 50.9% of the wound closures needed skin graft was and 15.4% needed amputation. Long hospitalization, pain during dressing and expenditure were also problems. For better outcome, nutrition support, proper dressing methods and early wound closure should be addressed.

Even when the wounds were healed, patients will suffered from late undesirable effects such as lymphedema, lymphangitis and limb deformity (Fig. 4) that prevented them from living a normal life for a long time. At the present day, prevention with vaccination would be answer[13].

Conclusion

In this study, gram negative organisms were predominant wound isolates whereas gram positive

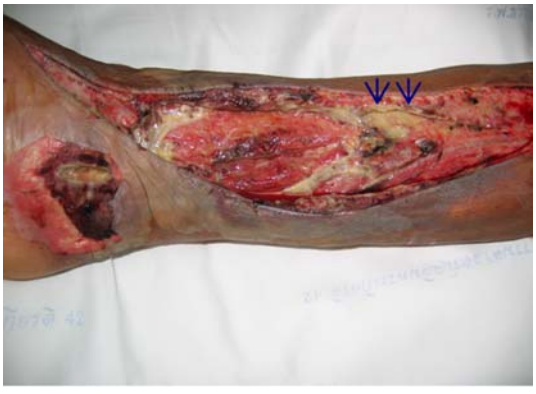

Fig. 3 Necrosis of superficial fascia (arrow)

Fig. 4 Deformity in necrotizing fasciitis patient with post-skin graft treatment

organisms were predominant blood isolates. Polymicrobial isolates were not predominant but high incident. The elderly and diabetic patients were in risk. Clinical manifestation can described as necrotizing fasciitis type I. Synergistic of various bacteria should be always be considered . Patients with fever, toxicity and erythematous swelling skin findings, the necrotizing fasciitis must be diagnosed early. Whenever it is suspected, surgery exploration is the only way of definite diagnosis. The hallmarks of treatment are prompt surgical opening and debridement to get rid of the source of infection and early broad-spectrum antibiotics treatment administrated.

Acknowledgements

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การศึกษาย้อนหลังของเนื้อเยื่อพังผืดอักเสบตาย ในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

สุรจิต อาวสกุลสุทธิ

วัตถุประสงค์*: เนื้อเยื่อพังผืดอักเสบตายเป็นการติดเชื้อเนื้อเยื่ออ่อนที่มีการดำเนินโรคเร็วและรุนแรง โดยหวังว่าความรู้ทางคลินิคและการวิเคราะห์เชื้อต้นเหตุจะช่วยลดอัตราตายและผลแทรกซ้อนจากการวินิจฉัยและการรักษาที่ล่าช้าได้*

วัสดุและวิธีการ*: เป็นการศึกษาทบทวนเวชเบียนของผู้ป่วยเนื้อเยื่อพังผืดอักเสบตายระหว่าง พ.ศ. 2547-พ.ศ. 2552 จำนวน 222 คน ที่รับการรักษาเป็นผู้ป่วยใน ในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ*

ผลการศึกษา*: มีสัดส่วนเพศชายต่อเพศหญิง 1.4:1 อายุเฉลี่ย 56.3 ปี กลุ่มอาชีพที่พบบ่อยคือผู้สูงอายุและกรรมกร ห้วงเวลาที่เกิดโรคชุกคือฤดูฝน เท้าและขาเป็นตำแหน่งที่เกิดติดเชื้อมากที่สุดและส่วนใหญ่ไม่ทราบสาเหตุนำ โรคร่วมที่พบบ่อยคือโรคเบาหวาน อาการนำที่สำคัญได้แก่รอยโรคที่ผิวหนัง 100% ไข้ 50.9% ช็อก 32.4% ผลเพาะเชื้อขึ้นได้จากแผล 55.9% และจากเลือด 48% พบเชื้อได้จากแผลส่วนใหญ่เป็นแบคทีเรียแกรมลบ 71.98% ส่วนเชื้อได้จากเลือดส่วนใหญ่เป็นแบคทีเรียแกรมบวก 51.28% ผลเพาะเชื้อที่ได้เชื้อมากกว่าหนึ่งชนิดจากแผล 48% และจากเลือด 6% หัตถการเพื่อการรักษาทำโดยการกำจัดเนื้อตาย 33.8% ปลูกผิวหนัง 59.9% และตัดอวัยวะ 15.4% จำนวนหัตถการเฉลี่ย 2.5 ครั้ง อัตราตาย 5.9% โดยเป็นผู้เป็นโรคเบาหวาน 46.2%*

สรุป*: ผลจากการเพาะเชื้อจากแผลพบส่วนใหญ่เป็นแบคทีเรียแกรมลบแต่ผลจากเลือดเป็นแบคทีเรียแกรมบวก โดยจากลักษณะที่พบเชื้อแบคทีเรียหลายชนิดร่วมกัน และลักษณะแสดงทางคลินิกจัดเป็น necrotizing fasciitis type I โดยกลุ่มเสี่ยงคือผู้สูงอายุและผู้เป็นโรคเบาหวาน ลักษณะสำคัญในการวินิจฉัยคือ ไข้ ลักษณะเลือดเป็นพิษและผิวหนังบวมแดง หลักการรักษาสำคัญคือการกำจัดแหล่งเชื้อโดยเร็วด้วยการผ่าตัด opening and debridement และการให้ยาปฏิชีวนะแบบ broad-spectrum*