LUPUS SCIENCE & MEDICINE™

Necrotising fasciitis in systemic lupus erythematosus: a case report and literature review

Y Tung Chen,[1] D Isenberg[2]

To cite: Tung Chen Y, Isenberg D. Necrotising fasciitis in systemic lupus erythematosus: a case report and literature review. *Lupus Science & Medicine* 2014;**1**:000008. doi:10.1136/lupus-2014-000008

Received 3 January 2014
Revised 13 April 2014
Accepted 22 April 2014

ABSTRACT

Necrotising fasciitis (NF) is a rare infection of the subcutaneous tissue, known to be rapidly progressive and potentially fatal. Patients with systemic lupus erythematosus (SLE) may be predisposed to this condition, and early clinical recognition can be difficult. We report a case of necrotising fasciitis in a 26-year-old woman with SLE. She presented with painful swelling of her left leg, then developed clinical features of septic shock. Emergency debridement was performed. Intraoperative findings revealed NF and cultures grew *Pseudomonas aeruginosa*. The patient survived after a lengthy hospital admission, following several further debridements complicated by recurrent chest sepsis and multiorgan failure. We also review and discuss the published cases of NF in SLE patients.

INTRODUCTION

Necrotising fasciitis (NF) is a serious soft tissue and life threatening infection, primarily involving the skin and superficial fascia, characterised by a rapid and extensive necrosis of the subcutaneous tissue. Most patients have associated comorbidities, such as diabetes, HIV infection or treatment with immunosuppressive drugs, but it can also affect previously healthy individuals. Infection is one of the common causes of morbidity and mortality in patients with systemic lupus erythematosus (SLE). It is associated with immunosuppressive agents, renal failure, and increased disease activity. Despite the increased propensity of SLE patients to develop common and opportunistic infections, NF has rarely been reported. To our knowledge, only 31 cases are described in the literature to date (see table 1). NF has also been described in other rheumatic diseases including polymyositis, dermatomyositis, systemic sclerosis, rheumatoid arthritis and ankylosing spondylitis, but it appears that this association is more common in SLE.[1 2]

We describe the case of a NF caused by *Pseudomonas aeruginosa,* complicated by recurrent sepsis and multiorgan failure in a young patient with a history of SLE.

CASE REPORT

A 26-year-old Asian woman with a complex history of SLE, diagnosed at age 14 years when she presented with malar rash, arthralgia, mouth ulcers, pulmonary vasculitis, strongly positive anti-nuclear antibody and anti-dsDNA antibodies. Subsequently, she had idiopathic detrusor overactivity with repeated urinary tract infection. Linked to her corticosteroid treatment she developed avascular necrosis of her elbow (at that time, on prednisolone 6 mg daily). The patient was also treated with hydroxychloroquine (HCQ), azathioprine (AZA) (100 mg from 1999 to 2009) and had 14 courses of cyclophosphamide (CYC) (a cumulative dose of 14 g) and two of rituximab (RTX) (two 1 g intravenous infusions separated by 2 weeks), the last being given in March 2012 for a SLE flare manifested by severe vasculitic rash. Immediately prior to B-cell depletion, her C3 level was 0.33 g/L (normal: 0.65–1.65), cluster designation (CD) 19 count was 0.146/µL (0.11–0.69), and immunoglobulin G level was 23.4 g/L (7–16).

In May 2012, she presented to her local hospital with painful swelling of her left lower limb, she denied a history of trauma, and her inflammatory markers and ultrasonography were normal, and she was discharged. Within 12 h she was found at home with a Glasgow Coma Scale of 6, and was admitted to the intensive care unit (ICU). On examination, the patient was in septic shock with hypotension (systolic blood pressure 60 mm Hg), tachycardia (135/min), and respiratory failure (SaO_2 70%). Poorly demarcated discolouration and blistering purpuric patches on her left lower limb were noted. Laboratory results showed erythrocyte sedimentation rate 96 mm/h (normal: 1–7),

[1]Department of Internal Medicine, University and Polytechnic Hospital of la Fe, Valencia, Spain
[2]Department of Medicine, Centre for Rheumatology, University College of London, London, UK

Correspondence to
Professor D Isenberg;
d.isenberg@ucl.ac.uk

Table 1 Clinical features of NF in systemic lupus erythematosus

n	Race/age/sex	Organ involvement	Medications	Comorbidities	Reported anaemia	Alb (gr/dl)	WBC (×103/mm^3) (Lym)	Classification of NF	Isolated micro-organism	Presentation	Outcome	Reference
1	A 26F	Lung and cutaneous vasculitis, myositis, Raynaud, thrombopenia, ART, hepatitis	CS, HCQ, CYC, RTX, Doxycycline	Detrusor overactivity, AVN of elbow, digital ischaemia. *Escherichia coli* urinary tract infections	Yes	1.7	15.4 (1.9%)	1	*Pseudomonas*	Leg pain, purpuraic patches	S	Current report
2	NA 39F	N, ART, thrombopenia	CS, HCQ	DM	No	NA	16.7 (NA)	1	Aeromonas	Leg pain, blisters	S	[1]
3	NA 28F	Cerebral lupus, N, ART	CS	Mental retardation, AVN hips	No	NA	10.5 (9.5%)	1	*Streptococcus*, Serratia marcescens, Aeromonas, Morganella	Leg pain, fever	S	[1]
4	Aboriginal 34F	N, APS	CS	Renal failure	No	3.3	7.0 (4.3%)	2	*Streptococcus*	Thigh skin sore	S	[4]
5	H 48F	Photosensitivity, oral ulcers, leucopenia, pleural effusion, haemolytic anaemia.	CS, anticoagulation.	PE, APS, DM.	Yes	NA	Normal	1	SA	Thigh swelling, pain	S	[5]
6	A 58F	NA	CS	Hepatitis C, cirrhosis	No	NA	21.6 (NA)	1	SA, Serratia	Swelling leg	D	[6]
7	A 28F	Anaemia	None	None	Yes	NA	17 (NA)	1	*Pseudomonas*	Facial swellling, pain, fever	S	[8]
8	H 34F	ART, seizures	CS	None	No	3.3	15.6 (2.6%)	2	*Streptococcus*	Leg pain, swelling	S	[9]
9	H 43F	ART, N	CS, CYC	None	No	2.2	1.6 (23%)	1	*Escherichia*	Leg pain and oedema	D	[9]
10	AA 53F	ART, N	CS	Hypertension	No	1.9	1.3 (23%)	1	*Pseudomonas, Enterococcus*	Thigh ecchymosis, bullous lesion	S	[9]
11	AA 12M	ART, N	CS	None	No	2.9	4.3 (28%)	1	*Streptococcus pneumoniae*	Neck pain, swelling	S	[9]
12	AA 20F	ART, vasculitis, haemolytic anaemia	CS, AZA, HCQ, napro-xen	None	Yes	NA	NA (NA)	2	*Streptococcus*	NA	S	[9]
13	H 30F	Vasculitis, neph	CS, AZA, HCQ	None	No	3.3	NA (0.5 ×103/mm3)	NA	NA	NA	S	[9]
14	H 38M	ART, rash	CS, ubupro-fen	None	No	2.9	7.6 (9.2%)	—	Negative	NA	S	[9]
15	H 57F	Neph, ART, cerebritis	CS	CAD, hypertension	No	2.2	25.6 (3.9%)	2	*Streptococcus*	NA	D	[9]
16	Canadian 30F	Serositis, purupura, ART, malignant hypertensio, N	CS, CYC	None	Yes	NA	NA (NA)	1	*Streptococcus pneumoniae*	Face and neck swelling, erythema	S	[10]

Continued

Table 1 Continued

n	Race/age/sex	Organ involvement	Medications	Comorbidities	Reported anaemia	Alb (gr/dl)	WBC (×103/mm^3) (Lym)	Classification of NF	Isolated micro-organism	Presentation	Outcome	Reference
17	NA 18F	NA	NA	Renal insufficiency. Respiratory tract infection	No	NA	NA (NA)	1	*Streptococcus pneumoniae*	Dyspnoea, dysphagia, neck stiffness	S	11
18	NA 38F	ART	CS, CYC	Transverse myelitis	No	NA	4 (8%)	1	Salmonella	Fever, lumbar pain	D	12
19	NA 46F	Alopecia, oral ulcers, photosensitivity, ART, rash, thrombopenia	Etodolac	NA	Yes	NA	3.7 (NA)	1	*Streptococcus pneumoniae*	Thigh swelling, tenderness, pain	D	13
20	A 35F	N, thrombopenia	CS	Diarrhoea	Yes	NA	15 (3%)	1	Salmonella	Fever, thigh pain, swelling and haemorrhagic bleb	S	14
21	French 66F	Anaemia	AZA	DM	Yes	NA	1.8 (NA)	2	*Streptococcus*	Abdominal pain, leg swelling, haemorrhagic bleb	D	15
22	NA 40M	N	CS	NA	No	NA	NA (NA)	1	Serratia	Leg cellulitis	S	16
23	NA 46F	Pleuritis, ART	CS	None	Yes	NA	2.1 (20%)	1–2	Gram-positive cocci in chains	Thigh ecchymosis, oedema, bullae	S	17
24	A 21F	N	CS	Chronic renal failure	No	2.3	16 (40%)	1	Bacteroides, Morganella	Bartholin abcess	S	18
25	A 31F	N, thrombopenia	CS, CYC	DM, chronic watery diarrhoea	Yes	1.9	6.1 (9%)	1	Salmonella	Arm pain, swelling	S	19
26	H 23F	NA	CS	Deeply carious tooth	No	NA	16.5 (NA)	2	*Streptococcus, Staphylococcus*	Dysphagia, dyspnoea, trismus neck pain, oedema	S	20
27	NA 21M	N	CS, RTX, plasma-pheresis.	TTP, mesenteric vasculitis, C. difficile-associated colitis	No	NA	NA	1	Acinetobacter	Flank and thigh pain	D	21
28	NA 36F	Raynaud, APS, heart block, aseptic meningitis	CS, HCQ	Hip AVN	No	NA	8.2 (8.5%)	2	*Streptococcus*	Back, abdominal pain, fever	S	22
29	NA 14F	NA	CS, AZA	NA	No	NA	NA (NA)	1	*Streptococcus pneumoniae*	Face and neck swelling, pain	S	23
30	A 40F	Photosensitivity, Raynaud, oral ulcer	CS, HCQ, AZA	Systemic sclerosis, cutaneous ulcers	Yes	NA	2.3 (NA)	1	*Enterobacter, Enterococcus*	Fever, pain on ischial áreas	S	24

Continued

Table 1 Continued

n	Race/age/sex	Organ involvement	Medications	Comorbidities	Reported anaemia	Alb (gr/dl)	WBC (×103/mm³) (Lym)	Classification of NF	Isolated micro-organism	Presentation	Outcome	Reference
31	AA 17F	N, ART, palatal ulcer	CYC, CS, MMF, HCQ, aspirin.	Breast abscess	Yes	1.4	2.1 (12%)	1	*Haemophilus*	Arm and thigh swelling, pain	D	25
32	NA 58M	Non-healing digital ulcers	CS and MTX	Diverticulitis	No	NA	33 (NA)	1	Non-haemolytic *Streptococcus, Bacteroides*	Swelling scrotum pain	S	26

A, Asian; AA, African–American; APS, antiphospholipid syndrome; ART, arthritis; AVN, avascular necrosis; AZA, azathioprine; CAD, coronary artery disease; CS, corticosteroid therapy; CYC, cyclophosphamide; D, died; DM, diabetes mellitus; F, female; FG, Fournier's gangrene; H, hispanic; HCQ, hydroxychloroquine; Lym, lymphocytes; M, male; MMF, mycophenolate; MTX, methotrexate; N, nephritis; NA, not available; NF, necrotising fasciitis; PE, pulmonary embolism; RTX, rituximab; S, survived; SA, *Staphylococcus aureus*; TTP, thrombotic thrombocytopenic purpura; WBC, white blood cells.

c-reactive protein 281 mg/dL (0–5), white blood cells 15 400/µL (3000–10 000) (97% neutrophils; 1.9% lymphocytes), haemoglobin 9.6 g/dL (11.5–15.5), platelet 50 000/µL (150 000–400 000), Na 138 mmol/L (135–145), creatine kinase 474 IU/L (26–140), urea 16.8 mmol/L (1.7–8.3), alamine transaminase 384 IU/L (10–35), total bilirubin 11 mg/dL (0.3–1.9), albumin 17 g/L (34–50), creatinine 290 µmol/L (49–92) and proteinuria 2.30 g/L (0–0,10). Anticardiolipin antibodies were negative. Her C3 level was 1.0 g/L (0.65–1.65), CD19 count was 0.001/µL (0.11–0.69), and immunoglobulin G level was 9.32 g/L (7–16).

She had aggressive debridement and a diagnosis of NF was made. Cultures of muscle tissue only grew *P aeruginosa*, resistant to piperazillin-tazobactam; therefore, she was treated with meropenem, teicoplanin and clindamycin. As her clinical condition gradually improved, the antimicrobial therapy was stopped by the 2nd week. However, 1 week later, she deteriorated, with thick yellowish sputum, fever, respiratory distress and the chest X-ray showed right consolidation. Ciprofloxacin and teicoplanin were empirically started, and the patient's clinical condition gradually improved. A week after this treatment had finished, the patient became worse with a new left lower lobe consolidation, so the antibiotic therapy was changed to ceftazidime. Her lupus flared with a marked malar rash over both cheeks, so her steroids (prednisolone) were increased to 20 mg per day and HCQ was restarted.

She was in the ICU from May to August 2012, but made a remarkable recovery and was discharged home with a steroid-tapering regimen and HCQ. Later, she developed two more SLE flares, which were treated again with CYC and RTX, achieving good response. At 18 months follow-up, there is no evidence of new recurrent or severe ongoing infections.

DISCUSSION

Since 1883, more than 500 cases of NF have been reported. Most patients with NF ranged from 38years to 44 years, with a male to female ratio of 2–3 : 1, and apparently an increased incidence in African and Asian countries.[3] The true incidence is not known (it is estimated to be approximately 0.4 cases per 100 000), with a reported mortality from 20% to as high as 80%.[3–5] The causative agents of NF vary and include two main categories, polymicrobial (type 1) and infection of group A streptococcal (type 2).

Patients with SLE have an increased risk of infections, due to immunological dysfunction and the use of steroids and immunosuppressive agents.[6] Other factors, such as the presence of a variant form of the Fc receptor are also believed to contribute to the risk of pneumococcal infection.[7]

NF due to *Pseudomonas* has very rarely been reported.[8 9] The clinical presentation of patients with NF may be deceptively benign at onset, and it may not be possible to

distinguish it clearly from minor soft tissue infections. Our patient was discharged from the original hospital before being admitted subsequently severely ill to University College Hospital. The lesion was rapidly progressive, probably due to her SLE, and the prolonged steroid treatment and recent administration of CYC and RTX might have increased the risk of infection. During the initial period, exploration of the wound may be necessary even before the diagnosis is clear, particularly in a patient who is clearly toxic.

In addition to the present case, the other 31 cases of NF in SLE patients that have been reported are summarised in table 1. The ages ranged from 12 years to 66 years, and 27 (84%) were female. Most of the patients reported were Asian (33%, 7 patients), 33% (7 patients) Hispanic and 19% (4 patients) African–American. The sites of infection included the upper or lower limb (60%, 17 patients), the face, neck or tongue (18%, 5 patients), the genital area (11%, 3 patients) and the abdomen (11%, 3 patients). NF Type 1 was identified in 22 patients (71%) and type 2 in 7 patients (23%), and when reported, the most common isolation was *Streptococcus* (50%, 16 patients). Most of the patients presented with intense pain, poorly demarcated erythematous, swollen lesions over the limbs and systemic inflammatory response; 28 patients (88%) were receiving corticosteroids and 7 HCQ (22%). Additionally, use of other immunosuppressive drugs has been reported (5 CYC, 5 AZA, 2 RTX, 1 mycophenolate, 1 methotrexate, 1 plasmapheresis) before or at the time of infection. Other associated conditions have been identified, including nephritis (54%; 15 patients of 28 reported), either during the current presentation or in the past, 13 (42%) had active disease (presumably those taking >20 mg prednisolone or equivalent per day), 76% (13 of 17 reported) had lymphopenia, 100% (12 out of 12 reported) low serum albumin levels and 12 (37%) had anaemia. Interestingly, before the admission, 9 (28%) reported a previous episode of infection: urinary, Bartholin abcess, diarrhoea, respiratory tract infection, carious tooth, colitis, hepatitis C, cutaneous ulcers (2), breast abscess and diverticulitis. Most patients responded to therapy, but 8 of the 32 patients died (25%), probably due to the infection or because of complications (such as sepsis or pulmonary embolism).

The case presented here and the literature reviewed suggests that active disease, nephropathy, lymphopenia, anaemia, low serum albumin levels, immunosuppressive therapy and significant infections in the past, may constitute risk factors for the development of NF in patients with SLE. A high index of suspicion for the diagnosis is required, and surgical exploration should not be delayed, especially during the early stages, to improve the prognosis of this devastating complication.

Contributors All authors have contributed equally to this work.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

REFERENCES

1. Mok MY, Wong SY, Chan TM, *et al*. Necrotizing fasciitis in rheumatic diseases. *Lupus* 2006;15:380–3.
2. Torralba KD, Quismorio FP. Soft tissue infections. *Rheum Dis Clin N Am* 2009;35:45–62.
3. Edlich RF, Long WB III, Gubler KD. Necrotizing fasciitis. 2013. http://emedicine.medscape.com/article/2051157-overview
4. Hassell M, Fagan P, Carson P, *et al*. Streptococcal necrotising fasciitis from diverse strains of Streptococcus pyogenes in tropical northern Australia: case series and comparison with the literature. *BMC Infect Dis* 2004;4:60.
5. Barcelos A, Silva C, Pereira da Silva JA, *et al*. Fasciíte Necrotizante e Lúpus Eritematoso Sistémico. 2003 [cited 2013 Oct 4]; http://rihuc.huc.min-saude.pt/handle/10400.4/641
6. Hashimoto N, Sugiyama H, Asagoe K, *et al*. Fulminant necrotising fasciitis developing during long term corticosteroid treatment of systemic lupus erythematosus. *Ann Rheum Dis* 2002;6:848–9.
7. Yee AM, Ng SC, Sobel RE, *et al*. Fc gammaRIIA polymorphism as a risk factor for invasive pneumococcal infections in systemic lupus erythematosus. *Arthritis Rheum* 1997;40:1180–2.
8. Kumar S, Kokate V, Patil M, *et al*. Facial necrotizing fasciitis disclosing systemic lupus erythematosus. *Indian J Dermatol* 2013;58:163.
9. Kamran M, Wachs J, Putterman C. Necrotizing fasciitis in systemic lupus erythematosus. *Semin Arthritis Rheum* 2008;37:236–42.
10. Hill MD, Karsh J. Invasive soft tissue infections with Streptococcls Pneumoniae in patients with systemic lupus erythematosus. Case report and review of the literatur. *Arthritis Rheum* 1997;40:1716–9.
11. DiNubile MJ, Albornoz MA, Stumacher RJ, *et al*. Pneumococcal soft-tissue infections: possible association with connective tissue diseases. *J Infect Dis* 1991;163:897–900.
12. Simeon-Aznar CP, Cuenca-Luque R, Solans-Laque R, *et al*. Fulminant soft tissue infection by Salmonella enteritidis in SLE. *J Rheumatol* 1990;17:1570–1.
13. Isik A, Koca SS. Necrotizing fasciitis resulting from Streptococcus pneumoniae in recently diagnosed systemic lupus erythematosus case: a case report. *Clin Rheumatol* 2007;26:999–1001.
14. Khawcharoenporn T, Apisarnthanarak A, Kiratisin P, *et al*. Salmonella group C necrotizing fasciitis: a case report and review of the literature. *Diagn Microbiol Infect Dis* 2006;54:319–22.
15. Gindre S, Dellamonica J, Couadau E, *et al*. Secondary Streptococcus pyogenes peritonitis following necrotizing fasciitis. *Ann Fr Anesthèsie Rèanimation* 2004;23:737–9.
16. Huang JW, Fang CT, Hung KY, *et al*. Necrotizing fasciitis caused by Serratia marcescens in two patients receiving corticosteroid therapy. *J Formos Med Assoc Taiwan Yi Zhi* 1999;98:851–4.
17. Mendez EA, Espinoza LM, Harris M, *et al*. Systemic lupus erythematosus complicated by necrotizing fasciitis. *Lupus* 1999;8:157–9.
18. Kohagura K, Sesoko S, Tozawa M, *et al*. A female case of Fournier's gangrene in a patient with lupus nephritis. *Nihon Jinzo Gakkai Shi* 1998;40:354–8.
19. Jidpugdeebodin S, Punyagupta S. Salmonella crepitant pyomyositis in a patient with systemic lupus erythematosus. *J Infect Antimicrob Agents* 2004;21:11–5.
20. Chrcanovic R, Custódio N. Cervical necrotizing fasciitis of odontogenic origin: case report. *Stomatol Glas Srb* 2009;56:194–200.
21. Charnot-Katsikas A, Dorafshar AH, Aycock JK, *et al*. Two cases of necrotizing fasciitis due to acinetobacter baumannii. *J Clin Microbiol* 2008;47:258–63.
22. Anderson JF, Cunha BA. Group A streptococcal necrotizing fasciitis of the psoas muscle. *Heart Lung J Acute Crit Care* 1999;28:219–21.

23. Patel M, Ahrens JC, Moyer DV, *et al*. Pneumococcal soft-tissue infections: a problem deserving more recognition. *Clin Infect Dis* 1994;19:149–51.
24. Chong J-H, Yoo W-H. Necrotizing fasciitis in a patient with overlap syndrome of systemic sclerosis and systemic lupus erythematosus. *Rheumatol Int* 2011;31:937–9.
25. Robinson AB, DeWitt EM, Schanberg LE, *et al*. Necrotizing fasciitis caused by Haemophilus influenzae type E in a 17-year-old girl with systemic lupus erythematosus. *J Clin Rheumatol Pract Rep Rheum Musculoskelet Dis* 2010;16:49–50.
26. Kearney DE, Harney S, O'Broin E, *et al*. An unusual presentation of Fournier's gangrene. *Ir J Med Sci* 2010;180:573–4.