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Early surgery for limb preservation in Group A *Streptococcus*-induced necrotizing soft tissue infection and subsequent soft tissue infection: A case report

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ABSTRACT

Background: Group A *Streptococcus pyogenes* (GAS) causes necrotizing soft tissue infections (NSTIs) necessitating exploration, surgical debridement, and possibly limb amputation.
Case presentation: A 45-year-old man presented with traumatic injury of the left carpal region, vomiting, and diarrhea. The swelling and pain in the left forearm worsened with sensorimotor deficits, and his skin color deteriorated. Emergent exploration was performed for limb preservation; GAS was detected in an exudate, and debridement was performed on postoperative day 2 for streptococcal toxic shock syndrome. He recovered uneventfully and was discharged; however, he returned after 2 months with GAS-induced STI at the same site and received antimicrobial treatment.
Conclusion: Exploration and subsequent debridement are crucial for effective treatment of NSTI.

Introduction

Invasive Group A *Streptococcus pyogenes* (GAS) infection is a lethal infection, with higher mortality rates for streptococcal toxic shock syndrome (STSS) [1]. GAS-induced soft tissue infections (STI) become necrotizing soft tissue infections (NSTI), which need early and complete surgical debridement of the infection site [1–3].

We report a case of GAS-induced NSTI of the upper limb and subsequent STI by a genetically similar GAS.

Case

A 45-year-old healthy man presented to the emergency department with worsening swelling and pain in the left hand, vomiting, and watery diarrhea. He had accidentally stabbed his left palm with a screwdriver 4 days before hospitalization.

On examination, he was conscious and had normal vital signs, except for a body temperature of 38.4 °C. Erythema and edema extending from the left forearm to the finger (Fig. 1A), with no wound exudation, were noted. The left radial artery pulse was palpable, and the nailbed capillary refilling time was less than 2 s. The left forearm swelling worsened and the skin tone deteriorated at admission in the emergency department (Fig. 1B). Pain worsened, and dysesthesia on the index and middle fingers appeared, with impaired volitional digital movements. The radial pulse was poorly appreciated, and blisters appeared over the distal upper limb. We conducted an emergency surgery to open the left carpal tunnel, without extensive dissection into the deep muscle. We observed an abundant exudate, without hematoma, abscesses, or visually identifiable necrotic tissue. Extensive soft tissue resection was not initially performed. The exudate and excised soft tissue were sent for Gram staining and culture. Gram-positive cocci were found in the exudate after Gram staining, but no bacteria was found on Gram staining of the soft tissue specimen. The exudate and blood cultures revealed GAS, although the tissue culture was negative. Penicillin G and clindamycin were administered.

Two days after the exploration, he developed tachycardia, hypotension, and truncal erythema. A blood test indicated renal impairment. An erythema over the left upper limb extended close to the shoulder joint. A second surgery was conducted (Fig. 2). The exudate had accumulated between the skin and soft tissue, and the

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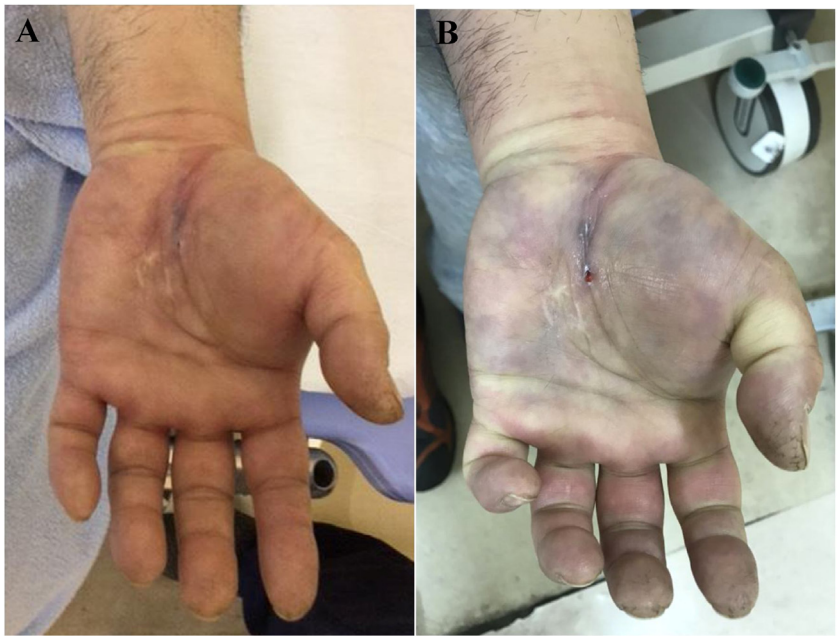

Fig. 1. (A) Findings from the left hand at hospitalization. A stab wound on the wrist (left carpal region) associated with redness and swelling from the wrist to the finger. (B) Findings in the left hand several hours after admission; there is increased swelling and deterioration of skin tone.

color of the soft tissue had deteriorated in some areas from the wrist to the forearm. Necrotic-appearing soft tissues were excised. A fasciotomy of the left arm was undertaken for a suspected NSTI.

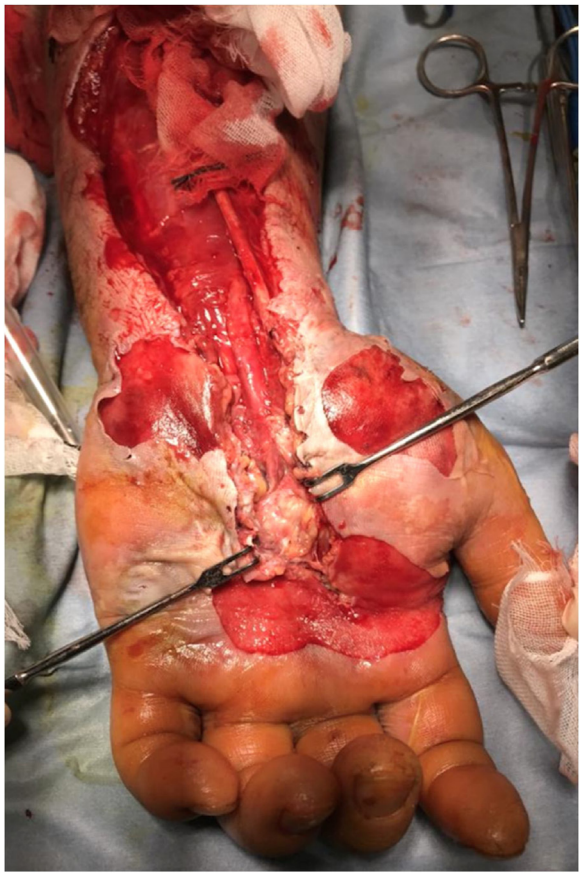

Fig. 2. Intraoperative findings from the second surgery. The exudate accumulated between the skin and soft tissue, and the color of the soft tissue had deteriorated in some areas from the wrist to the forearm. Necrotic-appearing soft tissues were excised.

Although surgical debridement of the necrotic fascia/muscle tissue was required, the muscles of the upper arm showed no signs of inflammation. Extensive muscle resection of the left upper arm was not performed. The exudate and resected soft tissue were collected for culture inspection and histopathological examination. Histopathology of the resected soft tissue showed neutrophilic infiltration and necrosis. Bacteria were not detected on cultures of the soft tissue and exudate. After the second surgery, an open wound management was performed. In the ICU, necrotic lesions were monitored daily for potential expansion; no additional debridement was subsequently required. He underwent four surgeries during hospitalization (including wound reconstruction) and received antimicrobials for 30 days. Antibiotic therapy duration was mainly determined based on local findings. We obtained negative blood cultures and did not repeat the blood and pharyngeal cultures after completing the antibiotic therapy. He was discharged on post-operatory day (POD) 53, with no sign of local inflammation. Follow-up observation of local findings was continued at the outpatient clinic, although CT and ultrasonography to check for abscess formation or infective endocarditis were not performed.

On POD 113, redness and swelling reappeared in the left hand. An NTSI or subcutaneous abscess was not suspected at the time of examination. An exudate was collected for culture by puncturing the dorsum of the left hand. He initially received oral cefaclor, but was switched to intravenous meropenem, clindamycin, and vancomycin intravenously after 5 days. GAS and *Staphylococcus aureus* were isolated from the exudate culture. He was switched to cefazolin and clindamycin based on the antimicrobial susceptibility for 14 days, followed by oral cefaclor. Antibiotic therapy was administered for 38 days. The local findings in the left forearm improved, and redness, swelling, or tenderness were not observed. There was no STI after completion of the antibiotic therapy.

We observed a genetic homology between GAS isolates from the blood in the first episode and pus in the second episode (Table 1). Genomic analyses revealed a similarity (%) in the strain type using 16S rRNA sequencing [4], *emm* type (subtype) with the full-length sequence [4], sequence type (ST) [4], streptococcal inhibitor of complement (*sic*) allele type [5], profile of exotoxin

Table 1
Phenotypic and genotypic features of *Streptococcus pyogenes* isolates from a patient with streptococcal toxic shock syndrome and the repetitive infection.

Isolation	The first isolate	The second isolate
Clinical specimen	Blood	Pus
Gross appearance of colonies on sheep blood agar plate	β-hemolytic white-colored smooth large colonies	β-hemolytic white-colored smooth small colonies
Numerical profile using the API-20 Strep system (% probability)	0161414 (99.9)	0161414 (99.9)
Similarity (%) of *S. pyogenes* type strain* using 16S rRNA sequencing (sequencing size, bp)	99.9 (1427)	99.9 (1417)
emm type (subtype)	*emm1*(.0)	*emm1*(.0)
emm full-length (sequencing size, bp)	99.9 % similarity to that of *S. pyogenes* MGAS5005 strain** (1090)	99.9 % similarity to that of *S. pyogenes* MGAS5005 strain** (1097)
Streptococcal inhibitor of complement (*sic*) allele No. (sequencing size, bp)	*Sic1.32* (935)	*Sic1.32* (941)
Sequence type (allelic profile: *gki-gtr-murI-mutS-recP-xpt-yqiL*)	28 (4–3-4–4-4–2-4)	28 (4–3-4–4-4–2-4)
Profile of exotoxin genes	*speA+speB+smeZ*	*speA+speB+smeZ*
Antimicrobial agent resistance class***	Macrolides (erythromycin and azithromycin)	Macrolides (erythromycin and azithromycin)
Profile of antimicrobial resistance genes	*mef*(A)	*mef*(A)

* *S. pyogenes* NCTC8198(T).
** Accession number is CP000017.2.
*** Resistance to antimicrobials was determined by the broth microdilution method according to the Clinical and Laboratory Standards Institute document M100-S22.

genes [4], and macrolide/lincosamide (ML) resistance determinants, including *erm*(A), *erm*(B), and *mef*(A) [5]. Both isolates were identical (99.9 % similarity) with regard to the 16S rRNA sequence in the NCTC 8198(T), *emm1*(.0) and the full-length sequence (accession number CP000017.2) of the MGAS5005 strain, ST28, *sic1.32*, exotoxin genotype of *speA–speB–smeZ*, and ML resistance genotype of *mef*(A), suggesting that both isolates had close genetic relatedness.

Discussion

Early debridement is important in NSTI treatment. However, the definition of "early" is unclear [1]. This controversy has originated from the various definitions of NSTI onset. The mortality rate of NSTI increases when the period between hospitalization and surgery exceeds 24 h [1,3]. The first surgery in our patient was undertaken approximately 7 h after hospitalization. Moreover, additional debridement should be undertaken at intervals of 6–48 h after the first debridement until no further necrosis or infected tissue is seen [1,2]. We conducted an additional debridement on POD 2; no further debridement was subsequently required. When the redness and swelling recurred on POD 113, an exudate was collected by puncturing the dorsum of the left hand and sent for culture. A good clinical course was achieved with antibiotic therapy alone. Retrospectively, however, surgical exploration, debridement, or continuous drainage could have been considered, given the possibility of a NSTI.

NSTI in the extremities may necessitate limb amputation for complete debridement of the infected site [2,3]. We considered left upper limb amputation because of the extension of erythema to the shoulder joint with STSS at the time of the second surgery. However, based on the intraoperative findings, which showed no signs of necrosis in the muscle tissue, extensive muscle resection of the left upper arm was not performed. The proportion of cases requiring limb amputation during NSTI treatment ranges from 8.4 % to a maximum of 46 % [3,6–8]. A retrospective study [6] on necrotizing fasciitis (NF) showed that diabetes, soft tissue swelling, skin necrosis, gangrene, and serum creatinine levels $\geq$1.6 mg/dL at admission were predictors of amputation. A retrospective study on NSTI [8] showed that the coexistence of heart disease, shock status, and infection with *Clostridium* spp. were predictors of amputation. Our patient showed only soft tissue swelling and skin necrosis, suggesting that adequate debridement without amputation can be undertaken in cases with a few predictive amputation factors.

Antibiotics were administered until local inflammation disappeared after the initial surgery; an STI caused by genetically similar GAS recurred at the same site 2 months later. A few cases of recurrent NF have been reported [9,10] and they had risk factors for NF, unlike in the present case. Three reasons for multiple STIs were identified: the initial exploration may have been inappropriate and early surgical debridement might have been unsuccessful, leading to a latent infection; the causative bacteria might have been latent in other parts of the body and could have reentered the affected site; the duration of antimicrobial therapy may have been suboptimal. To prevent multiple STIs, optimal antimicrobial therapy duration should be examined in a clinical study.

In conclusion, when considering the probability of NSTI, explorations and subsequent debridement should be considered.

Disclosures

Approval of the research protocol: N/A.
Informed consent: Written informed consent to publish the case report and accompanying images was obtained from the patient.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.

Declaration of Competing Interest

The authors report no declarations of interest.

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Not applicable.

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