Necrotising Soft Tissue Infections in Adults - Microbiology Full Clinical Guideline

Reference number: CG-ANTI/2019/068

Introduction

- Bacterial invasion of the soft tissues - with infective-inflammatory mediated occlusion of the vasculature - can cause necrosis of the skin (necrotising cellulitis), fascia (necrotising fasciitis), and/or muscle (necrotising myositis).
- Notable risk factors include diabetes mellitus and other immunocompromise (e.g. human immunodeficiency virus).
- Necrotising soft tissue infection can be divided into:
    - Type I: polymicrobial.
    - Type II: monomicrobial.
- Type I infections are caused by:
    - ≥ 1 anaerobe: e.g. *Bacteroides*, *Clostridium*, or *Peptostreptococcus* species; and
    - ≥ 1 facultatively anaerobic Gram positive coccus; and
    - ≥ 1 facultatively anaerobic Gram negative bacillus: e.g. *Escherichia coli*, *Enterobacter* species, *Klebsiella* species, or *Proteus* species.
- Type II infections are caused by:
    - 1 bacterial pathogen: e.g. beta-haemolytic streptococci (for example, *Streptococcus* group A/*Streptococcus pyogenes*) or *Staphylococcus aureus*.
- Invasion occurs with or without skin breach.
- Skin breaches can be secondary to:
    - Trauma: e.g. childbirth, injections of intravenous drug usage, insect bites, penetrating injuries, surgical incision.
    - Infection: e.g. varicella.
- Invasion without skin breach is associated with non-penetrating, minor injuries:
    - Muscle strain, ligament sprain, contusion, haematoma.
- Skin erythema, warmth, and oedema are manifestations that overlap with the symptoms and signs of erysipelas/cellulitis. Crescendo pain (severe, rapid, and requiring narcotic analgesia), dusky-purplish skin, skin bullae (haemorrhagic bullae), and crepitus can be distinguishing features of necrotising soft tissue infections.
- The life threatening nature of this infectious disease can also manifest in diagnostic criteria for sepsis and septic shock, e.g. hypotension.

Diagnosis

- If symptoms, signs, sepsis, and/or septic shock raise the differential diagnosis of necrotising soft tissue infection, immediately collaborate with the relevant surgical registrar/consultant on call.
    - Ophthalmology, maxillofacial, and/or otorhinolaryngology opinions can be required for the head and neck;
    - General surgery and/or obstetrics/gynaecology for the female torso;
    - General surgery and/or urology for the male torso;
    - Orthopaedics for the limbs.

- If surgery suspects necrotising soft tissue infection, surgical intervention is the overriding priority; superseding other management strands, e.g. completion of resuscitation.
- Necrotising soft tissue infection remains a surgically diagnosed infectious disease, and time is tissue for this life threatening infectious disease:
    - Specifically, National Confidential Enquiry into Patient Outcome and Death (NCEPOD) Classification of Intervention:
        - Code: 1.
        - Category: immediate.
        - Description: immediate (A) lifesaving or (B) limb or organ-saving intervention. Resuscitation simultaneous with surgical treatment.
        - Target time to theatre: within 30 minutes.
        - Expected location: next available operating theatre – "break-in" to existing lists if required.

- NB Microbiology nomenclature can be complex, with infectious diseases terminology reflecting pathogens, anatomy, pathophysiology, physicians, etc.
    - Necrotising soft tissue infection nomenclature includes clostridial anaerobic cellulitis, clostridial myonecrosis, Fournier's gangrene, gas gangrene, nonclostridial anaerobic cellulitis, synergistic necrotising cellulitis, and streptococcal myonecrosis terminologies/subtypes.

Pre-operative management

Investigation

- Blood sciences:
    - Full blood count (FBC), C reactive protein (CRP), lactate, urea and electrolytes (U&E), and liver function tests (LFT) may reveal markers of infection, sepsis, and organ dysfunction, and are recommended.
    - Aspartate aminotransferase or creatine kinase rises are suggestive of necrotising soft tissue infection, and are also recommended.
- Microbiology:
    - Blood cultures x 2-3 may reveal single or multiple pathogens, and are recommended.
    - Methicillin resistant *Staphylococcus aureus* (MRSA) screen is also recommended.
- Radiology:
    - Imaging is NOT recommended:
        - Diagnoses of necrotising soft tissue infection are established via surgical exploration in theatre.
        - Time is tissue for this life threatening infectious disease.

Treatment

- Empiric, intravenous antibiotics within 1 hour:
    - First line: piperacillin tazobactam 4.5 g 8 hourly and clindamycin* 1.2 g 6 hourly dual therapy.
        - If clinical concerns re the risk of MRSA, add teicoplanin 6 mg/kg (round up to the nearest 200 mg) intravenously 12 hourly for the first 24 hours, 6 mg/kg (round up to the nearest 200 mg) 24 hourly thereafter, target pre dose level 15-30 mg/l.
    - Second line, if non-immediate without systemic involvement penicillin allergy: meropenem 1 g 8 hourly and clindamycin* 1.2 g 6 hourly dual therapy.

        - If clinical concerns re the risk of MRSA, add teicoplanin.
    - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy: metronidazole 500 mg 8 hourly and ciprofloxacin 400 mg 12 hourly and linezolid 600 mg 12 hourly triple therapy.
        - NB Linezolid's spectrum includes MRSA.
    - * Clindamycin for 48 hours from the last return to theatre for debridement. Clindamycin thereafter requires consultation with the microbiology consultant on clinical duty.

Intra-operative management

Investigation

- Microbiology:
    - Surgical samples may reveal single or multiple pathogens. Fluid (≥ 1 ml), pus (≥ 1 ml), and/or tissue (~ 0.5 to 1 cm^3) specimens in universal containers for microscopy (white cell count and differential), culture, and susceptibilities (MC&S) are recommended.
    - Please notify the laboratory during the day (Queen's Hospital Burton, extension 4045; Royal Derby Hospital, extension 88218, option 2) or the microbiology biomedical scientist on call (via switchboard) to enable prompt processing of the surgical samples.

Treatment

- Surgical intervention:
    - In general:
        - Exploration ± debridement of necrotic soft tissues to macroscopically healthy, viable tissue ± amputation.
    - Specifically:
        - Reflecting possible ophthalmology/maxillofacial/ otorhinolaryngology/general surgery/obstetrics and gynaecology/urology/orthopaedic involvement:
            - Further specific intervention will vary from specialty to specialty:
                - For example, general surgery may intervene - via laparoscopy - with diversion stoma formation.

Post-operative management

Investigation

- ± Repeat microbiology:
    - Surgical sites can become colonised with human and environmental flora, especially with the administration of antibiotics.
    - Repeat sampling of the debrided surgical site is only recommended:
        - If returned to theatre; and
        - If there is surgical concern re ongoing necrotising soft tissue infection.

Treatment

- Intensive Care Unit (ICU):
    - Post-operatively, to be transferred from theatre to the ICU, with the anaesthetic consultant in theatres to liaise with the intensivist team re transfer of care.

- Surgical interventions:
    - Post-operatively, bacteria may remain within the macroscopically healthy, viable tissue. Therefore:
        - If clinical concerns emerge immediately:
            - Collaborate with the relevant surgical registrar/consultant on call regarding ± return to theatre.
        - If no clinical concerns emerge immediately:
            - Return to theatre ≤ 24 hours after the first/latest surgical intervention for re-inspection.
            - Return to theatre 24-48 hourly thereafter, until the surgical team are satisfied that no necrotic soft tissue remains.
    - With the nature of this infectious disease necessitating, in general, extensive debridement, early consultation with both plastic surgery (regarding reconstruction) and tissue viability are recommended.
- Antibiotics:
    - Empiric, intravenous antibiotics as per pre-operative management.
    - Directed, intravenous and/or per oral antibiotics in collaboration with microbiology.
    - Duration of antibiotics:
        - In general, 7 days from the last return to theatre.
        - NB1 Invasive group A streptococcal disease, ≥ 10 days from the last culture of *Streptococcus* group A/*Streptococcus pyogenes*.
        - NB2 Bacteraemia with *Staphylococcus aureus*, ≥ 14 days from the last blood culture of methicillin susceptible *Staphylococcus aureus* or MRSA.

Management summary

Differential diagnosis

- Symptoms (e.g. crescendo pain), signs (e.g. haemorrhagic bullae, crepitus), sepsis, or septic shock raising the differential diagnosis of necrotising soft tissue infection

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Diagnosis

- Immediate collaboration with the relevant surgical registrar/consultant on call
- If surgery suspects necrotising soft tissue infection, surgical intervention is the overriding priority
- Time is tissue: NCEPOD code 1 (immediate lifesaving/limb or organ-saving intervention within 30 minutes)

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Pre-operative investigation and treatment

- FBC, CRP, lactate, U&E, LFT. Aspartate aminotransferase or creatine kinase
- Blood cultures x 2-3. MRSA screen
- Empiric antibiotics within 1 hour:
  - First line: piperacillin tazobactam 4.5 g 8 hourly and clindamycin* 1.2 g 6 hourly dual therapy
    - If clinical concerns re the risk of MRSA, add teicoplanin 6 mg/kg (round up to the nearest 200 mg) intravenously 12 hourly for first 24 hours, 6 mg/kg intravenously 24 hourly thereafter, target pre dose level 15-30 mg/l
  - Second line, if non-immediate without systemic involvement penicillin allergy: meropenem 1 g 8 hourly and clindamycin* 1.2 g 6 hourly dual therapy
    - If clinical concerns re the risk of MRSA, add teicoplanin
  - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy: metronidazole 500 mg 8 hourly and ciprofloxacin 400 mg 12 hourly and linezolid 600 mg 12 hourly triple therapy
- * Clindamycin for 48 hours from the last return to theatre for debridement. Clindamycin thereafter requires consultation with the microbiology consultant on clinical duty

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Intra-operative and post-operative investigation and treatment

- Surgical exploration ± debridement ± amputation. Return to theatre ≤ 24 hours after the first surgical intervention for re-inspection. Return to theatre 24-48 hourly thereafter, until the surgical team are satisfied that no necrotic soft tissue remains
- Multiple fluid (≥ 1 ml), pus (≥ 1 ml), and/or tissues (~0.5 - 1 cm^3) in universal containers for MC&S
- Post-operative transfer to ICU
- Early consultation with both plastic surgery (regarding reconstruction) and tissue viability

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Document control

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