Intracranial Epidural Abscess in Adults - Microbiology Full Clinical Guideline

Reference number: CG-MICRO/2024/007

Introduction

- The commonest causes of intracranial epidural abscesses (IEA) are Gram positive and Gram negative bacteria.
- The specific causative agent varies with the mechanism of transmission.
- Pathogens (e.g. streptococci, *Haemophilus* species) can be inoculated through a contiguous mechanism of transmission. Another focus of infection (e.g. osteomyelitis, mastoiditis, otitis media, sinusitis) disseminates locally and invades the potential epidural space.
- The pathogens of IEA (e.g. staphylococci [including *Staphylococcus aureus*]) can also be inoculated directly via surgery or trauma; iatrogenic and traumatic mechanisms of transmission, respectively.
- Lastly, inoculation can be through a haematogenous mechanism of transmission. Microorganisms can disseminate via the blood (venous foramina of the frontal bone plate) and inoculate the potential epidural space.
- One of the potential outcomes of:
    - Microbial invasion of the potential epidural space; and
    - The subsequent inflammatory response

  Is the formation of an IEA.
- The IEA may manifest with fever, focal neurological deficit, headache, nausea, and/or vomiting.

Differential diagnosis

- The symptoms and signs of IEA can be mimicked by other intracranial lesions.
- Other infectious and non-infective mimickers include:
    - Brain abscess, infective encephalitis, meningitis, and subdural empyema.
    - Cranial arteritis, haematomas, intracranial tumour (both primary and metastatic), and meningiomas.

Investigation

Radiology

- First line: in general, computed tomography (CT).
- Second line: in general, magnetic resonance imaging (MRI); collaborate with the consultant radiologist.
- NB1 Within the Queen's Hospital Burton (QHB) and the Royal Derby Hospital (RDH), the CT service operates 24 hours per day, 7 days per week.
- NB2 Within the QHB and RDH, the MRI service operates 0900-1700 Mondays to Fridays.
- NB3 In the QHB, there is no MRI service out-of-hours.
- NB4 In the RDH, discussion with the medical consultant and – if the senior physician deems MRI essential – liaison with the on call radiology consultant is required 1700-0900 Mondays to Fridays, and all-day Saturdays and Sundays.

Microbiology

- With the range of microbial pathogens, variations in resistance and susceptibility profiles, contraindications, side-effects, and with prolonged durations of weeks-months of antimicrobial chemotherapy, microbiological investigation enables best antibiotic practice:
    - Before starting antimicrobials:
        - Blood cultures × 2.
    - If the neurosurgical team intervenes:
        - Aspirate/Biopsy for microscopy, culture, and susceptibilities (MC&S).
            - If the differential diagnosis includes tuberculosis, aspirate/biopsy also for acid-alcohol fast bacilli microscopy and *Mycobacterium* culture.

Histology

- With the differential diagnosis including intracranial tumors:
    - If the neurosurgical team intervenes:
        - Biopsy for neurohistopathology.

Blood sciences

- Full blood count (FBC), C-reactive protein (CRP), lactate, urea and electrolytes (U&Es), and liver function tests (LFTs).

Treatment

Please note:

- The antibiotic sections include fluoroquinolone usage.
- The Medicines and Healthcare products Regulatory Agency (MHRA) - with input from the Commission on Human Medicines (CHM) - have reviewed and published drug safety updates regarding systemic fluoroquinolones.
- Ciprofloxacin is hyperlinked to the British National Formulary.
- For NHS medicines and MHRA information for healthcare professionals on ciprofloxacin, click here and here, respectively.
- For MHRA printable information for patients on fluoroquinolones, click here.

Surgical intervention

- Neurosurgical intervention with:
    - Needle aspiration; or
    - Drainage

  Can be considered.
- With the variable:
    - Mechanisms of inoculation (contiguous, iatrogenic, traumatic, or haematogenous)
    - Locations of IEAs
    - Neurologic sequelae associated with neurosurgical intervention

  Ensure collaboration with the neurosurgery registrar/consultant on call in Nottingham.

Empiric, intravenous antibiotics

	First line	Second line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy
If there is: (i) no past medical	Metronidazole 500 mg 8	Chloramphenicol 25 mg/kg 6

history of acute or chronic otitis media; and (ii) if there are no symptoms, no signs, and no radiological findings of middle ear infectious disease	hourly **and** Ceftriaxone 2 g 12 hourly	hourly (NB maximums of 2 g 6 hourly and of 8 g within 24 hours)
If there is: (i) past medical history of acute or chronic otitis media; and/or (ii) symptoms, signs, or radiological findings of middle ear infectious disease	Meropenem 2 g 8 hourly	Metronidazole 500 mg 8 hourly **and** Ciprofloxacin 400 mg 8 hourly **and** Linezolid* 600 mg 12 hourly
If history of penetrating traumatic injury to the brain or post-operative (neurosurgery) IEA	Meropenem 2 g 8 hourly **and** Linezolid* 600 mg 12 hourly	Metronidazole 500 mg 8 hourly **and** Ciprofloxacin 400 mg 8 hourly **and** Linezolid* 600 mg 12 hourly
* If linezolid is contraindicated, vancomycin (dose as per hospital guidelines), target pre dose level 15-20 mg/l		

NB Chloramphenicol

Treatment regimens in adults	Central nervous system infection: chloramphenicol 12.5-25 mg/kg 6 hourly (NB maximums of 2 g 6 hourly and of 8 g within 24 hours)
Cautions	BNF: "With intravenous use avoid repeated courses and prolonged treatment"
Interactions	Please review the BNF for an up-to-date and comprehensive list of interactions
Rare or very rare side-effects	BNF: "With parenteral use **aplastic anaemia** (reversible or irreversible, with reports of resulting leukaemia)"
Renal impairment • GFR 25-50 ml/min • GFR 10-25 ml/min • GFR < 10 ml/min	 Dose as in normal renal function Dose as in normal renal function Dose as in normal renal function
Hepatic impairment	BNF: "With intravenous use… manufacturer advises caution (increased risk of bone-marrow depression) – monitor plasma-chloramphenicol concentration… manufacturer advises consider dose reduction"
Therapeutic drug monitoring (TDM) • Recommended • First TDM • Sample • Level • Repeat	 Yes, in discussion with the microbiology consultant Before and after 3rd or 4th dose 1-2 ml serum, pre and post (2 hours) dose Pre dose < 10 mg/l; post dose 10-25 mg/l 5-7 days

Directed, intravenous antibiotics (with susceptibilities)

- Case by case discussion between neurosurgery and microbiology is recommended.
- Specific bacteria can be associated with polymicrobial infectious disease. Therefore, microbiologists may recommend directed, intravenous antibiotics with spectrums of activity that extend beyond the cultured bacteria.

- *Streptococcus* species, according to susceptibilities:
    - First line: benzylpenicillin 2.4 g 4 hourly **±** metronidazole 500 mg 8 hourly (e.g. if culture of *Streptococcus anginosus*, *Streptococcus constellatus*, or *Streptococcus intermedius*).
    - Second line, if non-immediate without systemic involvement penicillin allergy: ceftriaxone 2 g 12 hourly **±** metronidazole 500 mg 8 hourly (e.g. if culture of *Streptococcus anginosus*, *Streptococcus constellatus*, or *Streptococcus intermedius*).
    - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy: linezolid 600 mg 12 hourly **±** metronidazole 500 mg 8 hourly (e.g. if culture of *Streptococcus anginosus*, *Streptococcus constellatus*, or *Streptococcus intermedius*).
- Anaerobes (e.g. *Bacteroides* species), according to susceptibilities:
    - First line: metronidazole 500 mg 8 hourly **and** ceftriaxone 2 g 12 hourly.
    - Second line, if ceftriaxone is contraindicated: meropenem 2 g 8 hourly.
    - Third line: collaborate with the microbiology consultant responsible for sterile site investigations.
- *Haemophilus* species, according to susceptibilities:
    - First line: ceftriaxone 2 g 12 hourly.
    - Second line, if ceftriaxone is contraindicated: meropenem 2 g 8 hourly.
    - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy:
        - In collaboration with the microbiology consultant responsible for sterile site investigations:
            - ± Ciprofloxacin 400 mg 8 hourly; **or**
            - ± Co-trimoxazole 960 mg 12 hourly; **or**
            - ± Chloramphenicol 25 mg/kg 6 hourly (NB maximums of 2 g 6 hourly and of 8 g within 24 hours).
- *Staphylococcus aureus*, according to susceptibilities:
    - First line: flucloxacillin 2 g 4 hourly.
    - Second line, if non-immediate without systemic involvement penicillin allergy: meropenem 2 g 8 hourly.
    - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy: linezolid 600 mg 12 hourly.
- Other bacteria and fungi:
    - Collaborate with the microbiology team.

Intravenous to per oral step down or outpatient parenteral antimicrobial therapy

- After 10-14 days of intravenous antimicrobial chemotherapy, if the patient is afebrile, observations stable, and inflammatory markers downward trending, collaborate with the neurosurgeon and microbiologist regarding (1) per oral step down or (2) outpatient parenteral antimicrobial therapy (OPAT).
- After 10-14 days of intravenous antimicrobial chemotherapy, if the patient is febrile, observations unstable, and/or inflammatory markers upward trending, collaborate with the neurosurgeon, radiologist, and microbiologist regarding re-imaging, further surgical intervention, and continue intravenous therapy.

Directed, per oral antibiotics (with susceptibilities)

- Case by case discussion between neurosurgery and microbiology is recommended. Please liaise with the neurosurgeon first and the microbiologist second.

- Specific bacteria can be associated with polymicrobial infectious disease. Therefore, microbiologists may recommend directed, per oral antibiotics with spectrums of activity that extend beyond the cultured bacteria.
- Please note, opinions vary regarding IEAs and per oral antibiotics. Variations from microbiologist to microbiologist reflect pharmacokinetic and pharmacodynamic principles and the relative weighting of these parameters:
    - In microbial infection with abscess formation, an antibiotic must first traverse the membranes of the endothelium, then diffuse through the interstitium, and then traverse a second membrane, that of the abscess.
        - Infection initiates an inflammatory response; the inflammation renders the interstitial fluid more viscous. The increase in viscosity decreases the amount of antibiotic transferred by diffusion.
        - The abscess is traversed through passive diffusion across the membrane - rather than pores - impairing the delivery of antibiotics. As the abscess forms and matures, the permeation of the membrane decreases, impeding the delivery of antibiotics.
        - In microbial infection with abscess formation, as the abscess matures, bacteria transition from the planktonic to the sessile state. The planktonic state of bacteria is preferable for antibiotics; active bacterial metabolism is integral to the mechanism of action for anti-bacterials and bactericide (e.g. turnover of peptidoglycan enables beta-lactam inhibition of transpeptidases to cause bacterial death). The slow growing bacteria of mature abscesses are less susceptible to antibiotics.
- One microbiologist may recommend OPAT for the patient in question; another microbiologist per orals.
- *Streptococcus* species, according to susceptibilities:
    - Microbiology may recommend: amoxicillin 1 g 8 hourly ± metronidazole 400 mg 8 hourly (e.g. if culture of *Streptococcus anginosus*, *Streptococcus constellatus*, or *Streptococcus intermedius*).
- Anaerobes (e.g. *Bacteroides* species), according to susceptibilities:
    - Microbiology may recommend: metronidazole 400 mg 8 hourly **and** amoxicillin 1 g 8 hourly.
- *Haemophilus* species, according to susceptibilities:
    - Microbiology may recommend: ciprofloxacin 500-750 mg 12 hourly **or** co-trimoxazole 960 mg 12 hourly.
- *Staphylococcus aureus*, according to susceptibilities:
    - Microbiology may recommend: linezolid 600 mg 12 hourly.
- Other bacteria and fungi:
    - Collaborate with the microbiology team.

Directed, outpatient parenteral antimicrobial therapy

- Collaborate with the OPAT consultant.

Empiric, per oral or outpatient parenteral antimicrobial therapy

- If symptoms/signs/radiology features of IEA, and the microbiology is negative, collaborate with a microbiologist regarding empiric options.

Duration of antibiotics

- Before discharge to the community, neurosurgery to collaborate with radiology regarding the timeframe for follow-up imaging.
- If for per oral step down or OPAT, monitor bloods (FBC, CRP, U&Es, and LFTs) weekly-fortnightly.

- Courses of antibiotics ≥ 6 weeks.

Management

Clinical concerns re IEA (fever, focal neurological deficit, headache, nausea, vomiting, etc.)

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Investigation

- Radiology:
  - CT head
- Microbiology:
  - Blood cultures × 2
- Blood sciences:
  - FBC, CRP, lactate, U&Es, and LFTs

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Collaborate with the neurosurgical registrar/consultant on call in Nottingham

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Treatment

- Empiric, intravenous antibiotics (please note, pages 2-3)

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Treatment

- ± Surgical intervention
  - Needle aspiration or drainage
    - Aspirate/Biopsy for MC&S and histology

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Treatment

- Directed, intravenous antibiotics (please note, pages 3-4) initially
- ± Directed, per oral antibiotics (please note, pages 4-5) latterly

References

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Document control

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