J R Coll Physicians Edinb 2006; **36**:232–235

Acute fever and headache – is it meningitis?

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ABSTRACT Acute fever and headache is a common clinical problem but clinicians need to remain vigilant with a high index of suspicion for acute bacterial meningitis. Even when the diagnosis is suspected clinically, the subsequent investigation and management is controversial. We discuss the diagnosis and management of these patients relevant to the acute medicine physician. The initial assessment should include severity assessment, as appropriate help can then be obtained early. In the absence of signs of raised ICP, shock, or respiratory failure, a diagnostic LP should be performed. If LP has to be deferred, CSF obtained up to 48 hours after antibiotics have been initiated may still lead to a diagnosis by PCR. Where LP is contraindicated, or it is anticipated that there will be a delay of more than 30 minutes, a dose of 2 g of intravenous cefotaxime or ceftriaxone should be given immediately. Brain imaging is not indicated in the majority of patients. Early treatment with appropriate antibiotics, fluid resuscitation, and management of raised intracranial pressure are key to improving patient outcome. Empirical antibiotic regimens should be guided by the age of the patient and risk factors for resistant pathogens. Microbiological advice should be sought early if there is any uncertainty. Adjunctive dexamethasone therapy for suspected bacterial meningitis should be administered either before or at the time of antibiotic administration.

KEYWORDS Acute fever, bacterial meningitis, diagnosis, headache, lumbar puncture, management

LIST OF ABBREVIATIONS Capillary refill time (CRT), cerebrospinal fluid (CSF), Consultant in Communicable Disease Control (CCDC), disseminated intravascular coagulation (DIC), ethylenediamine tetraacetic acid (EDTA), Glasgow coma score (GCS) intracranial pressure (ICP), lumbar puncture (LP), polymerase chain reaction (PCR), tuberculous meningitis (TBM), urinary tract infection (UTI)

DECLARATION OF INTERESTS No conflict of interests declared.

Published online ***April 2006***

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INTRODUCTION

The combination of acute fever and headache is a common clinical problem in the emergency department and medical admissions unit. The differential diagnosis for these symptoms is wide, ranging from a self-limiting viral infection to more serious life-threatening conditions like bacterial meningitis, severe sepsis, and brain abscess requiring specific management (see Table 1). When evaluating such patients, clinicians need to remain vigilant for the possibility of serious infections. It is preferable to over-treat and over-investigate than to miss the opportunity to intervene at an early stage.

Assessment should focus on identifying serious treatable causes of fever and headache thus enabling management to be targeted appropriately. This article will concentrate on the diagnosis and management of patients with suspected acute bacterial meningitis, but many of the principles discussed also relate to other infection-related causes of a fever and a headache. We will not discuss viral meningitis, which, in the absence of encephalitis, is typically a less serious, self-limiting condition.

TABLE 1 Causes of fever and headache.

- Viral infections without meningitis
- Meningitis
- Encephalitis
- Cerebral abscess
- Severe sepsis
- Non-specific symptoms of other infections, e.g. pneumonia, UTI, dengue, malaria, typhoid
- Local head and neck infections, e.g. sinusitis, tooth abscess, tonsillitis
- Non-infectious conditions, e.g. sub-arachnoid haemorrhage, cerebral venous thrombosis, pontine haemorrhage

INITIAL ASSESSMENT AND EARLY RECOGNITION OF SUSPECTED ACUTE BACTERIAL MENINGITIS

A high index of suspicion is needed in order to distinguish a case of meningitis from the many patients with febrile illnesses that present to the emergency departments. This can be a difficult exercise even for

TABLE 2 Warning signs in bacterial meningitis and meningococcal disease. These signs warn of impending or worsening shock, respiratory failure, or raised intracranial pressure and require urgent intervention.

- Rapidly progressive rash
- Poor peripheral perfusion, CRT >4 s, oliguria, or systolic blood pressure <90 mmHg (hypotension is often a late sign)
- Respiratory rate <8 or >30 breaths/min
- Pulse rate <40 or >140 beats/min
- Acidosis (pH <7·3) or base excess ≥5
- White blood cell count <4 x10^9/L
- Markedly depressed (GCS <12) or fluctuating (decrease in GCS >2) level of consciousness
- Focal neurology
- Persistent seizures
- Bradycardia and hypertension
- Papiloedema

experienced clinicians. Clues to the diagnosis may be obtained from a good clinical evaluation. In addition to fever and a headache, a history of neck stiffness and a change in mental status should be sought. Otitis media or significant head trauma in the past may reveal the entry point for the infection. Infectious contacts should be noted. Recent travel should raise the possibility of drug-resistant pathogens, e.g. penicillin-resistant pneumococci. Tuberculous meningitis should be considered in individuals with a sub-acute presentation and risk factors for TB, such as travel from an endemic area. Tuberculous meningitis or cryptococcal meningitis can be the defining illness for HIV infection and therefore an appropriate risk factors history should be obtained and a thorough physical examination undertaken, looking for features such as oral candidiasis, seborrhoeic dermatitis, oral hairy leukoplakia, lymphadenopathy, and a herpes zoster scar.

The clinical features of meningitis in its early stages are often non-specific. In some patients, the severity of the illness may be masked by prior administration of oral antibiotics in the community. However, once fully established, the characteristic features of meningitis are usually easy to recognise. Symptoms and signs of meningitis include fever, headache, neck stiffness, photophobia, nausea and vomiting, impaired or fluctuating mental status, focal neurology, and seizures. Patients may also complain of non-specific muscle aches and back pain. A petechial or purpuric rash is almost exclusively seen in meningococcal disease but, particularly in the early phases of the disease, the rash may be erythematous or maculopapular in character. Although the presence of a characteristic rash is highly suggestive of meningococcal infection, meningococcal septicaemia may occur in the absence of meningeal infection. On the other hand, as many as 50% of patients with proven meningococcal meningitis may not have a rash at presentation. No single clinical finding is sufficiently sensitive or specific to be diagnostic. The absence of fever, headache, and altered mental status can essentially exclude the diagnosis with a high negative predictive value but, individually, any of these features can be absent in patients with LP-proven disease. For example, 20–30% of patients with meningitis do not have neck stiffness at presentation.

TABLE 3 Specific contraindications to lumbar puncture in patients with meningitis.

Signs of raised ICP
Changing level of consciousness
Depressed level of consciousness
Focal neurological signs
Persistent seizures
Papiloedema[1]
Bradycardia and hypertension

Cardiovascular compromise
Impaired peripheral perfusion
Hypotension

Respiratory compromise
Tachypnoea
Abnormal breathing pattern
Cyanosis/hypoxia

Others
Coagulopathy[2]
Local skin sepsis

[1]Papiloedema is uncommon in bacterial meningitis even in patients with markedly raised ICP.

[2]In an immunocompetent patient with suspected community-aquired meningitis it is not routine to wait for a normal coagulation result before undertaking an LP. Clinically significant DIC will only occur in the context of septicaemia, in which case the LP is contra-indicated.

Early recognition of meningitis followed by prompt institution of therapy is central to improving patient outcome. Individuals who appear relatively well may deteriorate rapidly without warning. A revised management algorithm for adults has recently been developed by the British Infection Society (www.meningitis.org; www.britishinfectionsociety.org).

The initial clinical evaluation should include severity assessment, as appropriate specialist help can then be obtained early. This should include consideration of the patient's airway, breathing (respiratory rate and oxygen saturation), and circulatory status (pulse, urine output, capillary refill time). It is also essential to look for the warning signs of severe disease (see Table 2). The presence of one or more of these signs should prompt the clinician to seek assistance from the critical care team, as patients can deteriorate rapidly even once antibiotics are started. Care should be taken not to confuse shocked patients with meningococcal sepsis who have cerebral hypoperfusion in the absence of meningeal inflammation, with meningitis patients who have raised intracranial pressure.

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INVESTIGATION OF SUSPECTED ACUTE BACTERIAL MENINGITIS

All patients should have blood taken for a full blood count, blood glucose, urea and electrolytes, liver function tests, C-reactive protein, a clotting profile, blood cultures, and an EDTA blood sample for meningococcal PCR. A throat swab for culture should also be taken. In patients where shock is suspected, acid base status should be urgently assessed. In the absence of signs of raised ICP, shock, or respiratory failure, a diagnostic LP should be performed (see Table 3). If the LP has to be deferred initially, obtaining CSF up to 48 hours after antibiotics have been initiated may still lead to a diagnosis by PCR. Lumbar puncture provides confirmation of the diagnosis and bacteriological culture of CSF may yield the aetiology, antibiotic sensitivities, and provide important prognostic information.

It has become common practice to arrange for a CT brain scan to exclude raised intracranial pressure prior to undertaking a LP in patients with suspected meningitis. This approach is poorly supported by available evidence. Clinically significant raised ICP cannot be ruled out by brain CT and therefore a normal scan can be falsely reassuring. Meningitis patients presenting with clinical signs of raised ICP are the minority and should not undergo LP regardless of the CT findings. A CT brain scan may define a dural defect in adult patients with otitis media or mastoiditis. However, in the context of community-acquired meningitis a CT brain scan rarely identifies conditions requiring neurosurgical intervention such as cerebral abscess or hydrocephalus. Transporting patients to a CT scanner before they have been adequately stabilised is unsafe and may result in sudden deterioration in an uncontrolled environment. The inevitable delay in undertaking the CT scan requires that empirical antibiotics be given while awaiting the procedure, therefore impairing the diagnostic yield from a subsequent LP.

MANAGEMENT OF SUSPECTED ACUTE BACTERIAL MENINGITIS

Management should be guided by the clinical presentation. Fluid resuscitation should be started if there are signs of dehydration, poor peripheral perfusion, or shock (capillary refill time >4 seconds, oliguria, or hypotension with a systolic blood pressure <90 mmHg). Restriction of fluid, although previously recommended in central nervous system infections, may prejudice circulating volume and therefore cerebral blood flow. Circulatory shock should be resuscitated aggressively, significant dehydration addressed carefully to avoid fluid overload, fluid balance monitored frequently, and maintenance fluids should be given orally if possible. Unnecessary delay in the first dose of intravenous antibiotics should be avoided.

TABLE 4 Therapeutic recommendations for community-acquired bacterial meningitis.

Age group	Empirical antibiotic therapy
Adults 18–55 years	Cefotaxime 2 g six hourly or Ceftriaxone 2 g twelve hourly. *For suspected penicillin-resistant pneumococci* add vancomycin[1] 1 g twelve hourly ± rifampicin.
Adults > 55 years	Cefotaxime or ceftriaxone (as above) *plus* ampicillin 2 g four hourly or amoxicillin 2 g four hourly.

[1]Therapeutic levels should be monitored.

The level of consciousness should be documented and seizures treated appropriately, maintaining additional vigilance regarding the patient's airway. If there are signs of raised ICP, the patient would need critical care input for intubation and mechanical ventilation to facilitate oxygenation, to allow adequate sedation, and to permit normalisation of arterial PCO_2. Fluid balance should be monitored carefully and patients should be nursed head-up to maximise venous drainage. Intravenous mannitol reduces extracellular fluid accumulation and may be useful for managing acute changes in intracranial pressure and incipient coning. However rebound cerebral oedema may occur, necessitating further mannitol treatment. If bacterial meningitis is suspected, and LP is contraindicated, or it is anticipated that there will be a delay of more than 30 minutes, a dose of 2 g of intravenous cefotaxime or ceftriaxone should be given immediately. Except in cases where the patient is well and the diagnosis very uncertain, antibiotics should be administered empirically while awaiting the result of LP.

The selection of the optimal antibiotic for bacterial meningitis should be based on the spectrum of pathogens causing meningitis in different age groups, the changing pattern of antimicrobial resistance, the pharmacological properties of the antibiotics available; and the results of therapeutic trials. Current recommendations for initial antibiotic management for bacterial meningitis are shown in Table 4. Treatment should be intravenous throughout therapy and should be modified according to culture and sensitivity results. There should be close liaison between the clinician and the microbiology laboratory. Listeria monocytogenes is not susceptible to cephalosporins and therefore ampicillin or amoxicillin should be given in addition to a third generation cephalosporin in patients older than 55 years. If a patient is suspected of having a highly penicillin-resistant pneumococcus (recent travel to areas with high levels of penicillin-resistant pneumococci such as Southern Africa, Spain, the USA, and some Eastern European countries), vancomycin with or without rifampicin should be given in addition to a cephalosporin while awaiting further information from the laboratory.

J R Coll Physicians Edinb 2006; **36**:232–235

Adjunctive dexamethasone therapy for suspected bacterial meningitis, either before or at the time of antibiotic administration, has been adopted in many centres in North America and Europe. The cerebral injury that occurs in bacterial meningitis is largely due to a host-mediated inflammatory response. This process is triggered by the release of bacterial toxins and is exacerbated by antibiotic treatment. Until recently, in contrast to paediatric practice, there has been little evidence to support the routine use of steroid therapy in the management of adults with meningitis. A large multicentre, double-blind, randomised and placebo-controlled trial has shown a significant benefit in outcome (mortality and morbidity) with the administration of 10 mg dexamethasone together with, or within 20 minutes of, the first dose of antibiotic, and given every six hours for four days. Based on this study, the animal studies, the efficacy of dexamethasone in other forms of bacterial meningitis in children, and the lack of significant toxicity, we recommend adjunctive dexamethasone in all adult patients presenting with suspected or proven bacterial meningitis in the absence of known contra-indications, provided that antibiotic resistance is unlikely. Should an alternative diagnosis be made subsequently, the steroids can be stopped but we recommend continuing the dexamethasone for all causes of community-acquired bacterial meningitis. The benefit of steroid therapy underlines the importance of diagnostic LP in order to confirm the presumptive diagnosis.

All suspected cases of meningitis should be notified to the local CCDC, preferably within the first 12 hours. Contact tracing and prophylaxis will be undertaken in all cases of possible or proven meningococcal meningitis. To avoid confusion and unnecessary concern it is essential that all close contacts of the patient are managed by the CCDC in a co-ordinated manner rather than by members of the medical team. All index cases of meningococcal disease should also receive chemoprophylaxis unless they have been treated with ceftriaxone.

KEYPOINTS

- In a patient with acute fever and a headache, acute bacterial meningitis should be strongly suspected and appropriately managed.
- All patients should have a severity assessment and warning signs should prompt critical care team input.
- Lumbar puncture should be done in all cases unless contraindicated.
- Brain imaging is not indicated in the majority of suspected meningitis cases.
- Early treatment with appropriate antibiotics, fluid resuscitation, and appropriate management of raised intracranial pressure is key to patient outcome.
- Adjunctive dexamethasone therapy should be considered where bacterial meningitis is strongly suspected.

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