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A 25-Year-Old Female School Teacher from Malawi With Abrupt Onset of Fever and Confusion

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Clinical Presentation

History

A 25-year-old Malawian primary school teacher presents to a local central hospital. She was reported to be well at 8 a.m., confused by 10 a.m. and drowsy with a high fever and convulsions on admission at 11 a.m.

She is HIV-positive and has been on first-line antiretroviral therapy (ART) with tenofovir, lamivudine and efavirenz for 6 months with good adherence. Her CD4 count on starting ART was 320 cells/μL. She completed treatment for pulmonary tuberculosis 2 months ago.

Clinical Findings

The patient is restless and agitated; Glasgow Coma Scale 10/15. Pupils are equal and reactive with photophobia; the neck is stiff and there is no rash. Plantar responses are down-going, Kernig's sign is positive. Chest and abdominal examinations are unremarkable. Temperature 40°C (104°F), pulse 125 bpm, blood pressure 125/68 mmHg, oxygen saturation 93% on room air. During the physical examination she suffers a renewed seizure.

Laboratory Results

Her blood results are shown in Table 16.1. A spinal tap is done. The CSF appears hazy; CSF results are shown in Table 16.2. Rapid antigen test for *Plasmodium falciparum* is negative.

TABLE 16.1 Blood Results on Admission

Parameter	Patient	Reference
WBC ($\times 10^9$/L)	10.5	4–10
Neutrophil count ($\times 10^9$/L)	8.9	2.5–6
Haemoglobin (g/dL)	8.9	12–14
MCV (fL)	85	78–90
Platelets ($\times 10^9$/L)	255	150–400
Creatinine (μmol/L)	106	35–106
Random blood glucose (mmol/L)	5.6	3.9–7.8

TABLE 16.2 Results on Admission

Parameter	Patient	Reference
Leukocytes (cells/μL)	35 (60% neutrophils)	0–5/μL
Protein (g/L)	2.6	0.15–0.42
Glucose (mmol/L)	1.2	2.5–5

Questions

1. What are your treatment priorities for this woman?
2. What adjunctive interventions should be used in this setting?

Discussion

A 25-year-old Malawian woman, known to be HIV-positive and on ART, presents with acute severe symptoms including a high fever, a rapid decline in consciousness and new onset convulsions, suggesting a severe neurological infection. Her CSF is hazy and shows a neutrophilic pleocytosis, as well as a high CSF-protein and low glucose.

Bacterial meningitis is the most likely diagnosis; tuberculous meningitis and cryptococcal meningitis are possibilities, though much less likely, since they tend to present in a subacute manner.

Answer to Question 1

What Are Your Treatment Priorities for This Woman?

The suspected diagnosis is acute bacterial meningitis. In Africa *Streptococcus pneumoniae* is the most common cause of meningitis in adults and children. Additionally, in the meningitis belt, seasonal outbreaks of bacterial meningitis caused by *Neisseria meningitis* occur during the dry season. Case numbers have dropped considerably after the introduction of large-scale vaccination programmes.

The immediate treatment priority is emergency resuscitation, including rapid administration of antibiotics. A third-generation cephalosporin such as ceftriaxone at a high dose to penetrate the CSF is appropriate; where this is not available, high dose benzylpenicillin plus chloramphenicol is a suitable alternative. Resistance rates of *S. pneumoniae* to both penicillins and chloramphenicol are rising, hence local advice about resistance patterns should be sought. Data to guide resuscitation in adults are limited, but airway support and seizure control are indicated. Public health services are required for case management to ensure that appropriate vaccination programmes and case notification for outbreak monitoring are done.

Answer to Question 2

What Adjunctive Interventions Should be Used in This Setting and What Are Your Differential Diagnoses?

Several meta-analyses suggest that while in well-resourced countries dexamethasone should be given to adults and children presenting to hospital with meningitis, steroids should not be used in resource-limited hospitals in Africa given their lack of efficacy. Glycerol has been tested in paediatric meningitis with mixed results but was shown to be harmful in adults with meningitis in Malawi. No other adjuncts have been tested in clinical trials to date; adjunctive treatment is not indicated.

In cases of suspected meningitis, a lumbar puncture (LP) must be undertaken to obtain a diagnosis. Despite clinical contraindications to lumbar puncture in this patient (seizures and altered conscious level), the risk of causing harm by doing an LP is low. LP should not be delayed by attempts to obtain cerebral imaging unless obvious signs of a space-occupying lesion are present. CT scan of the brain is of limited value in bacterial meningitis. Administration of antibiotics should not be delayed while the LP is undertaken, particularly in resource-limited settings.

The main differential diagnoses for this patient are cryptococcal meningitis (CCM) and TB meningitis (TBM). However, her CD4 count is too high for CCM and her recent completion of TB treatment makes TBM less likely. In addition, both of these infections classically have a more chronic course.

She is not pregnant, therefore meningitis caused by *Listeria monocytogenes* is very unlikely. Bacterial pathogens that cause meningitis in HIV-infected adults include *S. pneumoniae,* group A streptococci, *Staphylococcus aureus,* invasive non-typhoidal salmonellae, *Salmonella typhi*, *Escherichia coli* and *Haemophilus influenzae;* all will be treated with a third-generation cephalosporin. European guidelines recommend 14 days of antibiotics in HIV-infected adults with bacterial meningitis. However, in sub-Saharan Africa often shorter courses are given, determined by the patient's recovery rate, local guidelines and availability of antibiotics for long courses. In children with bacterial meningitis in Malawi, 5 days of ceftriaxone was shown to be non-inferior to ten days, with substantial savings shown, and shorter courses are now commonly used.

The Case Continued…

In the emergency department the patient received ceftriaxone 2 g IV, 10 mg of diazepam IV and 600 mg of phenobarbitone IV. Her oxygen saturation improved with resuscitation. She received 10 days of IV ceftriaxone and recovered consciousness by day 3. CSF culture grew *S. pneumoniae.* Audiometry revealed a minor hearing loss in her right ear. No further neurological impairment or seizures were noted; anticonvulsants were weaned by day 3.

SUMMARY BOX

Acute Bacterial Meningitis

In resource-rich settings, acute bacterial meningitis in adults and children is declining in incidence because of successful vaccination campaigns, but sporadic cases continue to occur. In contrast, many countries with high HIV prevalence have reported an increase in patients presenting with acute bacterial meningitis (ABM) since the start of the HIV epidemic.

Case fatality rates in resource-rich settings have declined from 45–50% to 11–25% over the past 50 years, associated with early administration of broad-spectrum antibiotics and better supportive care. In contrast, adult ABM lethality rates in sub-Saharan Africa are reported to vary between 50 and 70% without any change over time, and survivors experience higher rates of neurological disabilities.

Adjunctive treatments have failed to reduce lethality in large randomized controlled trials in Africa despite efficacy elsewhere. In well-resourced settings, important risk factors for poor outcome include advanced age, hyperglycaemia and immunosuppression. In Africa, coma, seizures, anaemia and delayed presentation to hospital are poor prognostic features. Antibiotic treatment depends on local sensitivities. A third-generation cephalosporin at high dose given as early as possible is the treatment of choice.

Further Reading

1. Heckmann JE, Bhigjee AI. Tropical neurology. In: Farrar J, editor. Manson's Tropical Diseases. 23rd ed. London: Elsevier; 2013 [chapter 71].
2. van de Beek D, Cabellos C, Dzupova O, et al. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect 2016;22(Suppl 3):S37–S62.
3. Wall EC, Mukaka M, Denis B, et al. Goal directed therapy for suspected acute bacterial meningitis in adults and adolescents in sub-Saharan Africa. PloS One 2017;12(10)e0186687.
4. van de Beek D, Farrar JJ, de Gans J, et al. Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data. Lancet Neurol 2010;9(3):254–263.
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