Ward Round: Three children admitted to QECH, Blantyre

L Mankhambo, A Phiri, K Chiwaya, J Waluza, ES Borgstein, SM Graham

1. Department of Paediatrics and MLW Clinical Research Programme, and
2. Department of Surgery College of Medicine, Blantyre, Malawi

Corresponding author: Dr SM Graham FRACP, mulanje_45@yahoo.com

Case 1 - A boy aged 2 years 7 months

This boy presented with a two-week history of fever, cough and lethargy, and worsening dyspnoea for two days. He had been admitted a week earlier to a peripheral hospital for four days with the same complaints but he continued to deteriorate and so his mother discharged him and brought him to QECH for assessment.

Past medical history: previously well, fully immunized child with no known contact with tuberculosis (TB).

Examination

- a well-nourished boy (weight 12 kg; weight-for-height >85%)
- comatose with a non-localising withdrawal response to painful stimuli only
- pale, T 38.3ºC, pulse 160/min, BP 80/60 mmHg
- severe respiratory distress - respiratory rate 60/min, grunting, nasal flaring and subcostal indrawing. Oxygen saturation 79% on air
- reduced breath sounds and bronchial breathing on the right side
- hepatosplenomegaly 6 cm each
- no focal neurological signs
- cardiac examination normal

Initial investigations

- blood glucose 2.6 mmol/L: (normal 3.5-6.5) - corrected with a bolus of intravenous
- serum lactate (15.2 mmol/L: normal < 4.0).
- thick blood film: 1 – 10 asexual Plasmodium falciparum per high-power field
- packed cell volume (PCV): 13%.
- cerebrospinal fluid (CSF)(traumatic) white cells 5/mm3, red cell count of 1600/mm3, protein 30mg/dL and glucose 99 mg/dL (normal 60-120); culture – no growth
- HIV test - negative

Initial diagnoses and treatment

- Δ pneumonia and severe malarial anaemia
- Rx chloramphenicol 25mg/kg, a loading dose of quinine (20mg/kg) by slow infusion, oxygen by nasal prongs, whole blood transfusion (20ml/kg)

Progress

- after 5 hours the patient became unresponsive with lack of withdrawal to painful stimuli, brisk deep tendon reflexes, a fixed upward gaze, acidotic breathing and hypoglycaemia. He was given dextrose and parenteral gentamicin (6mg/kg/day) was added.
- by day 3 he was fully conscious and eating; PCV 26%, thick films negative for malaria
- Blood culture: Staphylococcus aureus, resistant to penicillin and chloramphenicol but sensitive to gentamicin, erythromycin, tetracycline and cotrimoxazole.
- Day 4: increasing respiratory distress, with dullness on percussion over the right chest. Chest Xray: diffuse opacification on right; Chest ultrasonography: 4 cm effusion in the right chest
- Pleural aspirate revealed an empyema. Rx cloxacillin; surgical consultation
- The same night, he developed repeated prolonged generalized seizures and became comatose. Blood glucose: normal.
- Rx oxygen, paraldehyde, ceftriaxone (100 mg/kg/day).
- Chest tube inserted - drained 400ml of thick pus, growing Staphylococcal aureus.
- Over the next 3 weeks, the patient remained comatose, with only a withdrawal response to painful stimuli
- developed decubitus ulcers
- developed a broncho-pleural fistula with a persistent collapsed right lung despite effective drainage. Recurrent chest drain obstruction required four replacements.
- CT scan of head – see Fig 1
- On day 24, he required another blood transfusion. On day 30, his fever began to settle. He became more responsive and was able to feed orally but had right-sided weakness. An ophthalmologist assessment on day 32 revealed marked visual loss and sluggish pupils but normal fundi.
- second CT scan with contrast – see Fig 2

Final outcome

The treatment was continued and he was discharged on day 54 with 1 week's supply of cloxacillin having already received cloxacillin for 7 weeks. At follow-up one month later, his progress was excellent. He was walking normally, feeding well, talking and his eyes were able to fix and follow.

Case 2: A 6 year-old girl

This child presented with a history of fever, headache and neck stiffness for 3 days and generalized seizures for a day. She was fully immunized including BCG immunization. The only remarkable history was of bilateral chronic suppurative otitis media for a year. She had no history of TB contact.

Examination

- Thin (weight 17 kg), alert, well perfused.
- T 38.7ºC, pulse 136/min, respiratory rate 34/min, BP 100/70 mmHg.
- Neck stiffness ++
- Right lateral gaze preference; generalised symmetrical brisk reflexes.
- Bilateral chronic suppurative otitis media

- Tender left mastoid, but no swelling of the mastoid
- Blood film negative for malarial parasites
- Blood glucose 6.5 mmol/L, blood lactate 5 mmol/L
- Lumbar puncture: CSF white cells 15/ul, no red cells, protein100mg/dL, glucose 252mg/dL, gram stain: no organisms seen.
- HIV test negative. Blood culture negative.
- Rx ceftriaxone (100mg/kg per day)

Progress

- On day 3 she started improving and her temperature settled.
- On day 5 she became irritable, confused and was unable to sit.
- Chest X-ray revealed right perihilar infiltrations
- Tuberculin skin test gave a blistering reaction of 20mm after 48 hours.
- Rx TB meningitis treatment and prednisolone 2mg/kg daily
- On day 10, a protruding left ear and a swelling over the left mastoid was noted.
- CT scan – see Fig 3

Final outcome

Surgeons were consulted and opted for a conservative approach with ceftriaxone, metronidazole (7.5mg/kg 8 hourly) and cloxacillin (25mg/kg 6 hourly). The TB meningitis treatment was discontinued. The patient responded and was discharged on day 29 on oral ciprofloxacin and flucloxacillin for 3 weeks.

Case 3 - An 11-year old boy

This boy was referred from a district hospital by the medical staff, where he had been admitted for a week after presenting with headache and fever for 4 weeks. At the district hospital, he tested positive for malaria and was treated with intravenous quinine, and he was given benzylpenicillin and chloramphenicol for suspected bacterial meningitis. Four days later while in the district hospital, he developed a left sided hemiparesis with left sided focal seizures, and was then referred to QECH for further management.

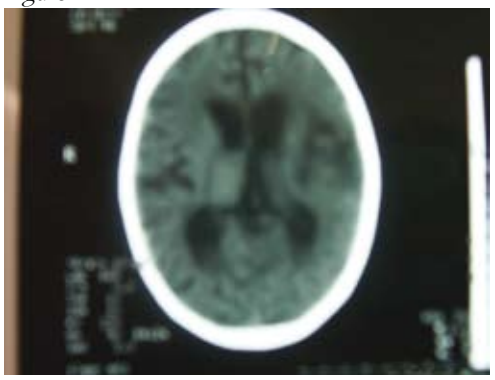
Assessment on admission to QECH

- A previously well boy, fully immunized with no history of TB contact.
- T 37.5C, BP 115/80 mmHg, respiratory rate 28/min, pulse rate 73/min
- Alert, well perfused
- Neck stiffness +; Kernig's sign positive
- Left sided hemiparesis. Direct ophthalmoscopy: bilateral disc 'fullness'
- Lumbar puncture: CSF under low pressure, white cell count of 18/mm3, red blood cell count 10/ul, protein 100mg/dL, glucose 252mg/dL, Gram stain negative
- Rx intravenous ceftriaxone (100mg/kg/day)
- On day 2, stable, afebrile; CSF culture result – no growth.
- Ceftriaxone was discontinued.
- HIV test – negative; tuberculin skin test - non-reactive after 72 hours.
- Cranial CT – see Fig 4.

What are the diagnoses in these three cases?
What lessons can we learn from these patients?

Turn to page 131 for a discussion of these cases

Figure 1



Figue 2

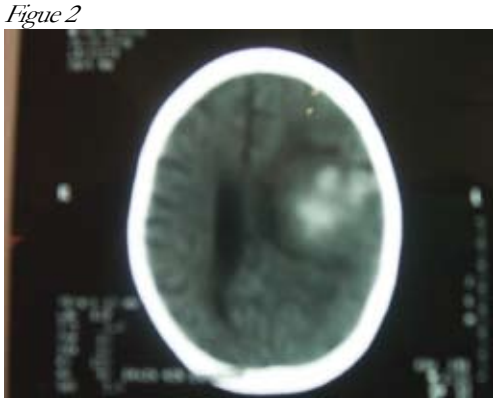


Figure 3

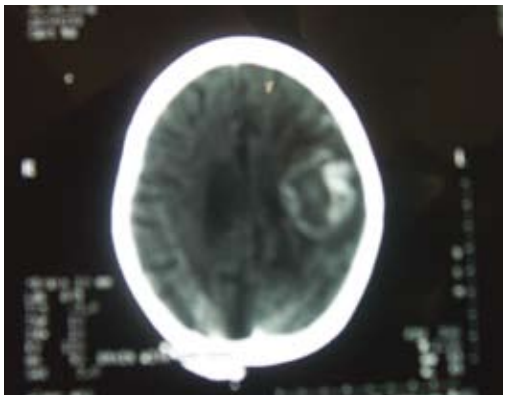
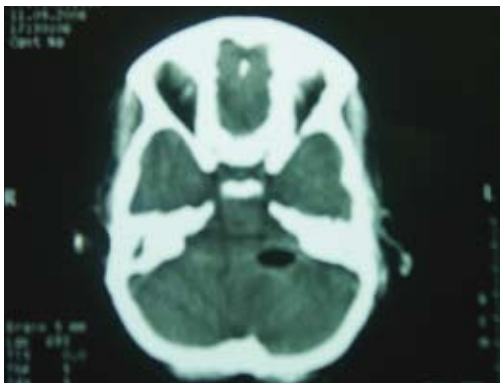


Figure 4



Ward Round: three children admitted to QECH, Blantyre

Continued from page 123

Cases 1-3 all suffered from various forms of intracranial abscess. Patients 1 and 2 both had a happy outcome. Case 3 was more problematic. The large subdural abscess shown in Fig 4 was surgically drained, but over the next 10 weeks further abscesses appeared elsewhere in the right hemisphere of the brain, requiring repeated surgical drainage and prolonged therapy with metronidazole and ceftriaxone. Although making some improvement, the child died a week after discharge from hospital.

The CT scans:

Case 1 – Fig 1 shows a lesion in the left parietal-temporal region; this was initially reported as 'consistent with a haemorrhage'. But the second scan (Fig 2), with the help of enhancement, showed a lesion with enhanced margins consistent with a brain abscess.

Case 2 – Fig 3 shows air and a lesion in the posterior fossa, with midline shift of the cerebellum and dilated ventricles; in the context the lesion is likely to be a pyogenic abscess.

Case 3 – Fig 4 shows a right subdural abscess measuring 3.5 x 2.5 cm, with midline shift.

Suppurative brain abscess is uncommon in children. Recent retrospective studies from tertiary referral hospitals in Pakistan and Australia reported 30 cases each over a ten-year period.[1,2] Most cases occurred in children over 4 years, case-fatality was 10-16% and the majority of survivors had long-standing neurological deficit. A recent review states that 25% of all brain abscesses occur in children under the age of 15 years with a peak at 4-7 years and a high morbidity and mortality.[4] Brain abscess is likely to be underreported from Malawi where diagnostic imaging is usually not available.

The pathogenesis of brain abscess was recently reviewed.[4,5] Infection can arise either directly from a contiguous site such as middle ear, sinuses, teeth, and compound skull fractures or indirectly via haematogenous spread from extracranial sources such as pulmonary infection, endocarditis or septicaemia. Organisms involved in children include *Streptococci* (anaerobic and aerobic) responsible for about 50-70%, staphylococci (10-30%) and enteric bacteria (10-25%).[4,6] Mixed flora can be found in up to 30%. The location and predisposing condition of the abscess influence aetiology.[4,5] Abscesses arising from sinus or odontogenic foci tend to be frontal and caused by streptococci (aerobic and anaerobic), enterobacteriaceae, Staphylococcus aureus and anaerobes. Temporal or cerebellar lesions are usually otic in origin with mixed flora that include aerobic and anaerobic *streptococci, Enterobacteriaceae* and *Pseudomonas aeruginosa*. Abscesses caused by haematogenous spread are usually due to a single pathogen (*Streptococcus milleri* and S*taphylococcus aureus* are important causes) and occur in the distribution of the middle cerebral artery.[3-5] A wider range of pathogens can cause brain abscess in immunocompromised children including fungi and mycobacteria.[5,6]

The three cases presented on page 131 were all previously well HIV-uninfected children. In two cases, a likely source of infection was identified – one with *staphylococcal* pulmonary infection and one with chronic suppurative otitis media and mastoiditis. The location of the abscesses was consistent with these associations. The one case with subdural empyema did not have an obvious extracranial source of infection.

A causative pathogen was not isolated from the abscess in any of the cases. It could be presumed in case 1 that the cause was *Staphylococcal aureus* as it was cultured from blood and pleural fluid. This was why cloxacillin was used for 8 weeks. Ceftriaxone was also used because of concerns that the brain abscess might be a complication of Salmonella septicaemia because at initial presentation case 1 had severe malarial anaemia as well as severe pneumonia. Severe malarial anaemia is commonly associated with bacteraemia due to non-typhoidal Salmonella with a risk of focal sepsis such as Salmonella meningitis or pneumonia following discharge.[7,8]

All three children had clinical features consistent with the presentation of a brain abscess[4,5] at the time the diagnosis was considered – fever, seizures and altered mental state. It is possible that earlier drainage of the staphylococcal empyema might have reduced the risk of brain abscess in Case 1 although it is also possible that the acute but temporary neurological deterioration that occurred 5 hours after admission correlated with the beginning of infective cerebritis which later evolved to become an abscess. Case 1 was also complicated with multiple pathologies which may have contributed to the neurological deterioration on day 6 before the chest drain was inserted. He had had malaria, severe anaemia, staphylococcal septicaemia and hypoxia although had been stable for some days. TB meningitis was considered in Case 2 because of lack of response to what is usually very effective antibiotics for bacterial meningitis (i.e. ceftriaxone) and it is usual to consider that diagnosis in those circumstances especially with some leucocytes in the CSF and a reactive TST. The diagnosis of brain abscess was entertained when the mastoid swelling was noted and in retrospect, the finding of a tender (though not swollen) mastoid on admission should have been considered more carefully.

These cases highlight the value of having CT scan for more accurate diagnosis. The presentation of fever, seizures and altered mental state is very common in children admitted to QECH. The commonest causes are cerebral malaria and acute bacterial meningitis. A positive blood film for malaria does not necessarily mean that the cause of coma is cerebral malaria[3] and a negative blood film does not necessarily exclude the diagnosis. The diagnosis of cerebral malaria is strongly supported by characteristic findings on examination of the fundus[9] so that other diagnoses should be more strongly considered if malarial retinopathy is absent. However, malarial retinopathy may not always be present with cerebral malaria and its recognition requires some training and experience. Bacterial meningitis is usually a straightforward diagnosis as long as there is a high index of suspicion and microscopy of CSF is available. Once cerebral malaria and

bacterial meningitis have been excluded or there is a poor response to treatment for the same, other diagnoses are usually considered including viral encephalitis, TB meningitis and brain abscess. Children with TB meningitis will usually have typical CSF findings of lymphocytosis and elevated protein while the CSF findings for brain abscess that has not ruptured into a CSF compartment are non-specific with overlap of findings with acute encephalitis. The three cases reported had only 5 to 18 white cells per mm^3 in the CSF.

The possibility of clinical overlap with other conditions that require different management emphasizes the value of available imaging such as CT scan, preferably with contrast as abscesses show a typical ring enhancement – this is shown in Fig 2. The use of contrast is not routine with cranial CT at QECH (and contrast is not always available) but ideally if brain abscess is considered, contrast should be used as it shows a characteristic enhancement of the abscess margins. Imaging is also required to direct surgical intervention which is an important part of the management.[4,5] In carefully selected patients, surgical drainage is required in patients with illness for >2 weeks, neurologically impaired with signs for raised intracranial pressure and abscesses > 3 cm. Minimal invasive surgery with CT or MRI guided stereotactic aspiration have replaced traditional open craniotomies for aspiration in the developed world. Surgery can reduce the raised intracranial pressure and aid to obtaining pus for microbial diagnosis and enhance antibiotic efficacy.

Cranial ultrasound is another imaging technique that is much more readily available than CT scan but its use is limited to children with open fontanelles. Ultrasound is useful for diagnosis of subdural collections as they tend to be more common in children under 2 years of age.[2] This diagnosis is not uncommon in our setting where the usual cause is non-typhoidal Salmonella (unpublished observation, SM Graham) and repeated needle aspiration through the fontanelle is part of management. The typical age range of brain abscess is in older children[2,3] and so ultrasound is not often helpful for diagnosis.

The management of brain abscess in children is challenging. The existence of other diseases with similar signs and symptoms can delay the diagnosis. The most valuable tools in this setting are: (1) to have a high index of suspicion for brain abscess, (2) to assess carefully for risk factors such as chronic ear disease or cardiac disease, and (3) to refer the patient promptly to a centre with adequate support that includes prolonged broad-spectrum antibiotics and surgical drainage. The availability of neuroradiological imaging is extremely useful for accurate diagnosis and effective management.

References

1. Leotta N, Chaseling R, Duncan G, Isaacs D. Intracranial suppuration. J Pediatr Child Health 2005; 41: 508-512
2. Mehnaz A, Syed AU, Saleem AS, Khalid CN. Brain abscess in children. Ind J Pediatr 2006; 73: 401-404
3. Taylor TE, Fu WJ, Carr RA, et al. Differentiating the pathologies of cerebral malaria by postmortem parasite counts. Nature Med 2004; 10: 143-145
4. Yogev R, Bar-Meir M. Management of Brain Abscess in Children. Pediatr Infect Dis J 2004; 23: 157-159.
5. Sáez-Llorens X. Brain Abscess in Children. Semin Pediatr Infect Dis 2003; 2: 108-114
6. Brook I. Brain Abscess in children: microbiology and management. J Child Neurology 1995;10:283-8.
7. Bronzan RN, Taylor TE, Mwenechanya J, et al. Bacteremia in Malawian children with severe malaria: prevalence, etiology, HIV coinfection and outcome. J Infect Dis 2007; 195: 895-904
8. Mankhambo L, Chiwaya K, Phiri A, Graham SM. Lobar pneumonia caused by nontyphoidal Salmonella in a Malawian child. Pediatr Infect Dis J 2006; 25: 1190-1192
9. Beare NAV, Taylor TE, Harding S, Lewallen S, Molyneux ME. Malarial retinopathy: a newly established diagnostic sign in severe malaria. Am J Trop Med Hyg 2006; 75: 790-797