Interactive clinical cases

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Warnings

1. All cases are true cases
2. Some may not be infectious encephalitis
3. Focus on cases where ‘something had to be done’
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1. All cases are true cases
2. Some may not be infectious encephalitis
3. Focus on cases where ‘something had to be done’
4. I have to catch a train at 10.23 AM
Case 0. Complicated cholecystectomy

A previously healthy, 67-year-old man

Story

- Elective cholecystectomy for cholelithiasis on June, 15th
- June 17th: T = 38.5°C, headache, altered mental status, nuchal rigidity
- Contrast-enhanced brain CT scan normal

CSF clear - Cytology

- 150 white cells/mm³
- 75% neutrophils
- Protein, 2 g/L
- Glucose, 2 mmol/L (serum, 4.5 mmol/L)

Bacteriology negative (direct examination)
Case 0. Complicated cholecystectomy

Initiated on iv amoxicillin, 12 g/day + aciclovir, 10 mg/kg x 3

June 20th (day 3) : worse (T = 39°C) – altered consciousness
- Contrast-enhanced Brain MRI normal
- Redo CSF – not clear anymore
  - 500 white cells/mm³, 75% neutrophils
  - Protein, 3 g/L - Glucose, 2 mmol/L (serum, 4.5 mmol/L)

Patient intubated / transferred to the ICU / T = 40°C on day 5

Microbiology negative
- 72 h cultures and PCR pneumo/meningo, ARNr16S, HSV (x 2), VZV
=> aciclovir discontinued

The wife wants to see you!
Case 0. Complicated cholecystectomy

Patient was fine until he arrived in the hospital

Last year, he had a strange story
- Pharyngitis
- Amoxicillin, 1 g x 2/day (oral)
- Initially better
- After a few days,
  - Headache
  - Fever
  - ‘strange behaviour’
- GP suggested that it may be drug-related, amoxicillin discontinued
- Cured within a few hours

⇒ Amoxicillin discontinued, patient improved in 24 h

NB: amoxicillin part of perioperative prophylaxis for gallblader surgery
Case 0. Learning point (1)

Drug-Induced Aseptic Meningitis

Over 200 cases reported in the literature

- Mostly ‘post-marketing’
- Delay 2-7 days post introduction
- Acute neutrophilic meningitis
- Encephalitis signs not rare (30%)
- No diagnostic test
  - Rely on medical history
  - Exclude other causes
  - ‘Accidental’ re-introduction
Drug-Induced Aseptic Meningitis

Four main classes of drugs:
- NSAIDs (mainly ibuprofen, especially in women with SLE)
- Antibiotics (> 50 cases reported)
  - Cotrimoxazole first
  - Penicillins second
- IgIV (if perfusion too fast)
- Monoclonal antibodies (OKT3)

Prognosis
- Improves fast once treatment discontinued
- If not diagnosed and treatment continued?
Case 1. A strange bank boss (1)
A previously healthy, 47-year-old man

Story
- Settings: biggest ever enterovirus meningitis outbreak in France
- Patient was fine until June, 10th
- Progressive headache since June, 11th
- Noticed fever on June, 13th
- Went to the E.R. by himself on June, 14th, because of untractable headache

Admission
- Body $T^\circ = 38^\circ$C
- Nuchal rigidity
- Oriented, no deficit
A strange bank boss (2)

Lumbar puncture

CSF clear

Cytology
- 150 white cells/mm³
  - 75% lymphocytes
  - 20% neutrophils
- 52 red blood cells

Biochemistry
- Protein, 1 g/L
- Glucose, 2.3 mmol/L (serum, 5 mmol/L)

Bacteriology negative (direct examination)
Provisional diagnosis of enterovirus meningitis
What to do with him?
A strange bank boss (4)

Was admitted, after much discussion

Pain killer

No antibiotic or antiviral

Surveillance 48 hours
- CSF cultures + PCR enterovirus
- Clinical monitoring

First night, 2 hours AM
- Call from the night nurse
- Urinated behind the radiator

What to do?
Still enterovirus meningitis?

- Aciclovir, i.v., 10 mg/kg, t.i.d., 14 to 21 days
- Call the micro lab to test for HSV PCR in CSF
- Admission in the ICU, despite ‘no organ failure’
- EEG: no seizures
- No control CSF
  - HSV-1 documented (PCR CSF)
  - Improved fast - left ICU at day 3
- Final outcome (> 10 years F-U)
  - Left the bank, became a singer, divorced, ‘happier life’
Learning points – case 1

1. Initial diagnosis often wrong
   - Reconsider when new events and/or new informations

2. Meningitis and encephalitis very close
   - Signs of encephalitis may be somewhat delayed

3. The danger of ‘benign’ meningitis outbreak
   - Each acute CNS infections must be considered seriously
   - At least in adults
Case 2. A very old lady (1)

92-year-old woman

Co-morbidities
- Horton vasculitis -> prednisone, 10 mg/day x 10 years
- Diabetes mellitus
- Lives in long term care facility – no relatives

Story
- A 5 days story of fever, headache, anorexia; 3 days of cough
- On admission, right basal crackles, $T^\circ = 39^\circ C$
- Altered mental status, sleepy, gag (nausea) reflex altered
- CXR ‘unclear’
  -> amoxicillin-clavulanate for suspected inhalation pneumonia
  ‘not to be reanimated’ order
A very old lady (2)

Day 2

- Still T° = 39°C, although crackles not heard anymore
- CXR normal
- Facial palsy / Ophtalmoplegia / mental status worse
- Brain CT scan (contrast-enhanced) normal
- Call to the LTCF: fully alert, loves life
A very old lady (3)

Lumbar puncture

CSF turbid ‘rice water’

Cytology
- 550 white cells/mm³
  - 55% lymphocytes
  - 45% neutrophils
- 2 red blood cells

Biochemistry
- Protein, 2 g/L
- Glucose, 2 mmol/L (serum, 7 mmol/L)

Bacteriology negative (direct examination)
A very old lady (3)

Lumbar puncture

CSF turbid ‘rice water’

Cytology
- 550 white cells/mm³
  - 55% lymphocytes
  - 45% neutrophils
- 2 red blood cells

Biochemistry
- Protein, 2 g/L
- Glucose, 2 mmol/L (serum, 7 mmol/L)

Bacteriology negative (direct examination)

1. What do you suspect?
2. Additional investigation(s)?
3. Empirical treatment?
MRI: Rhombencephalitis
MRI: Rhombencephalitis

Blood culture Gram + rods
CSF PCR negative for *Listeria*
A very old lady (4) : Outcome

i.v. Ampicillin, 200 mg/kg/day x 21 days
Gentamicin 3 mg/kg o.d. x 7 days

Corticosteroids discontinued / Diabetes controlled (insulin)

One month stay in the ICU
- 12 days mechanical ventilation
- Gag reflex slow to recover
- Ventilation-associated pneumonia

Went back to the LTCF
- Full recovery
Learning points – case 2

1. Initial diagnosis often wrong
   - Beware of ‘easy diagnosis’ in elderly (urine, respiratory)

2. High yield of blood cultures in listeriosis
   - 2, to be sampled before ATB (to rule out endocarditis, too)

3. Listeria rhombencephalitis: strange disease
   - Facial nerves palsies
   - Very old or very young / immunocompromised
   - Sub-acute presentation
   - Epidemiology ‘settings-specific’: know yours!
     - Almost none in the US and the UK
     - 10% of documented infectious encephalitis in France (46% †)
Case 3. A ‘fulminant encephalitis’

A healthy, 17-year-old man

Story
- Was fine until yesterday night (high school ‘alright’)
- Complained of severe headache / went to bed without dinner
- His mother could not wake him up the morning after
- Called emergency mobile unit -> Coma (GCS 6) / glycemia 5 mmol/L
- Intubated, brought to the ICU

Admission
- Body $T^\circ = 39^\circ C$
- Blood pressure 110/70 mmHg
- Not sedated, GCS = 6
- Rash
What do you do, right now?
CT scan before LP?
1. CT scan before LP in patients suspected of acute CNS infection if
   - Immunocompromised (including HIV)
   - Recent CNS disease
   - Seizures (< 1 week)
   - Altered consciousness (GCS < 11)
   - Focal neurological sign

2. Should never delay treatment (including steroids and ATB)
Fulminant ‘encephalitis’

Treatment (emergency)
- Dexamethasone, 10 mg x 4/day
- Cefotaxime, 300 mg/kg/day continuous infusion (loading dose, 50 mg/kg over 1 hour)

Microbiological diagnosis
- Blood cultures (twice within 10 minutes)
- Skin biopsy (culture, PCR)

Imaging
- CT scan or MRI (whatever is available first)
Final diag: Meningococcal meningitis

1. Host
- Young (< 25 years), no comorbidities

2. Chronology
- Fulminant (50% ‘perfectly fine’ 24 hours before)

3. Purpura
Purpura + meningitis = meningococcus

Not rare if looked for:
176/683 bacterial meningitis (26%)
- Meningococcus = 162/257 (63%)
- Pneumococcus = 8/352 (2.3%)
Patient died within 12 hours of admission

Blood cultures and skin PCR yielded *Neisseria meningitidis* serotype C

**Learning points – case 3**

1. **Meningitis and encephalitis very close**
   - Signs of encephalitis may occur early in fulminant meningitis

2. **If disease fast, be fast!**
   - Antibiotics at home, no matter documentation
Case 4. A crazy young woman (1)

A previously healthy, 17-year-old woman

Story
- Described by relatives as ‘strange’ since last month
- Diagnosis of atypical ‘mood disorders’ => paroxetine
- Seizures (no personal or family history)

Admission
- Body T° = 38°C – enlarged lymph nodes
- Status epilepticus
- ICU, seizures resolved on phenytoin
- Contrast-enhanced CT scan and MRI normal
- Movement disorders (orofacial dyskinesia – constant chewing)
- Altered mental status
A crazy young woman (2)

Lumbar puncture

CSF clear

Cytology
- 100 white cells/mm³
  - 85% lymphocytes
- 2 red blood cells

Biochemistry
- Protein, 1.2 g/L
- Glucose, 4 mmol/L (serum, 7 mmol/L)

Bacteriology negative (direct examination)
A crazy young woman (2)

Lumbar puncture

CSF clear

Cytology
- 100 white cells/mm³
  - 85% lymphocytes
- 2 red blood cells

Biochemistry
- Protein, 1.2 g/L
- Glucose, 4 mmol/L (serum, 7 mmol/L)

Bacteriology negative (direct examination)

1. What do you do?
2. What do you want to know?
3. Additional investigation(s)?
A crazy young woman (3)

Mother interviewed

- Never left France
- Never had boyfriend
- Nothing to declare among relatives
- No leisure activities (worked a lot)
- No special diet
- Plays a lot with the kitten, bought 3 months earlier
A crazy young woman (4)

Diagnosis
- Serum IgG *Bartonella henselae* 1/800 (N < 1/100)
- PCR CSF *B. henselae*

Treatment (28 days)
- Doxycyclin, 200 mg/day
- Ceftriaxone, 2 g/day

Outcome
- Fever, movement disorders and seizure resolved
- Psychiatric condition improved
Learning points – case 4

1. Extensive interview of the relatives
   *They may have the answer!*

2. When disease slow, even late treatment is of value

3. *Bartonella henselae* encephalitis
   - Ask about the kitten
   - Mostly children or young adults
   - Slow progression
   - Psychiatric presentation, seizures, movement disorders
   - Treatment: doxycyclin and/or ceftriaxone
Case 5. Comatose homeless (1)

A 37-year-old man

‘frequent flyer’ of the emergency ward
- Alcohol intoxications (5 g/L)
- And/or trauma (while drunk)

Brought by the firemen for coma in the street
- Alcohol 2 g/L
- $T = 38.5^\circ C$ – GCS = 9

Contrast-enhanced cranial CT scan
- ‘unchanged’ (atrophia)

‘wait until he wakes up’
- Ringer lactate
Comatose homeless (2)

The morning after: $T = 39^\circ C$, $GCS = 8$

Lumbar puncture

CSF clear

Cytology
- $50$ white cells/mm³
  - $80\%$ lymphocytes

Biochemistry
- Protein, $1$ g/L
- Glucose, $4$ mmol/L (serum, $6$ mmol/L)

Bacteriology negative (direct examination)
Comatose homeless (2)

The morning after: $T = 39^\circ C$, GCS = 8

Lumbar puncture

CSF clear
Cytology
- 50 white cells/mm$^3$
  - 80% lymphocytes
Biochemistry
- Protein, 1 g/L
- Glucose, 4 mmol/L (serum, 6 mmol/L)
Bacteriology negative (direct examination)

1. What do you suspect?
2. Additional investigation(s) ?
3. Empirical treatment ?
Aciclovir/amoxicillin i.v. high doses

Final diagnosis

Primary HIV infection
- HIV serology ELISA +
- Ag p24 + / Western Blot 2 bands
- HIV viral load in serum: 6 million copies/mL, in CSF 100 000 copies
- Tested negative 3 months earlier

No co-infection

Combined ARV (nasogastric tube, then orally)
- Darunavir/r + emtricitabine + tenofovir
- Fever and coma resolved within 1 week
- Admitted unprotected sex with N. K. (known HIV+, not treated)
Learning points – case 5

1. If no story, focus on treatable diseases
   - Including HIV, for sure (and syphilis +++)

2. Beware ‘easy diagnosis’ in homeless / alcoholic

3. MRI, and ask your neuro-radiologist
Case 6. When everything goes wrong (1)

A 47-year-old farmer

Story

- Severe seronegative rheumatoid arthritis (10 years)
- Stabilized with prednisone, 50 mg/day (5 years)
- Progressive weight loss (- 20 kg in last 2 years)
- Chronic diarrhea (1 year)
- Dyspnea (6 months) -> severe mitral regurgitation (3/4)

Pre-operative check-up

- Memory disorders for 3 months + ataxia + mood disorders
- T = 38°C
- CRP = 20 mg/L - 6 sets of blood culture sterile

Transferred to the ID department to ‘rule out’ ID
Brain MRI (1)
Brain MRI (2)
Case 6 – When everything goes wrong

Lumbar puncture

CSF clear

Cytology
- 20 white cells/mm³
  - 90% lymphocytes

Biochemistry
- Protein, 1 g/L
- Glucose, 4 mmol/L (serum, 6 mmol/L)

Bacteriology negative (direct examination)
Case 6 – When everything goes wrong

Lumbar puncture

CSF clear

Cytology
- 20 white cells/mm³
  - 90% lymphocytes

Biochemistry
- Protein, 1 g/L
- Glucose, 4 mmol/L (serum, 6 mmol/L)

Bacteriology negative (direct examination)

1. What do you suspect?
2. Additional investigation(s)?
3. Empirical treatment?
Case 6 – When everything goes wrong

Final diagnosis: Whipple disease

All PCR CSF negative, but:

Duodenal biopsy
- Macrophages, PAS +
- PCR *Tropheryma whippelii* +

Dramatic improvement (including brain MRI), with:
- One month ceftriaxone
- One year cotrimoxazole

Excised mitral valve
- PCR ARN 16S: *Tropheryma whippelii* +
Learning points – case 6

1. Extra-neurological symptoms are not here ‘just to distract’
   - They may be the most valuable clue
   - They may even bring the diagnosis (when CNS tests fail)

2. Some infectious diseases may be missed, even through well conducted modern studies
   - Those with no serological tests available
   - Those with limited meningeal involvement
   - Those we don’t think about, or we don’t know yet
Bonus – case 7

60 year-old-woman
Transferred from Zambia
‘full-blown’ AIDS
Pneumocystosis
Cryptosporidiosis
Wasting syndrome
Initial improvement
ARV
Parenteral nutrition
Secondary
Altered mental status
Ophtalmoplegia, nystagmus
Severe memory disorders
CSF ‘normal’ (prot 0.5 g/L)
Thank you!