Interactive clinical cases

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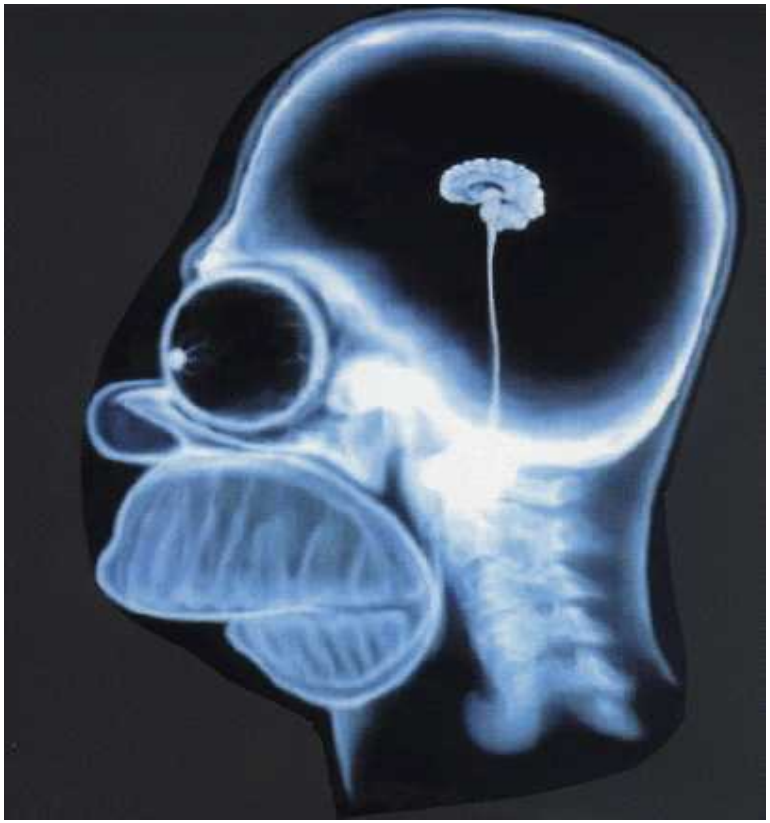
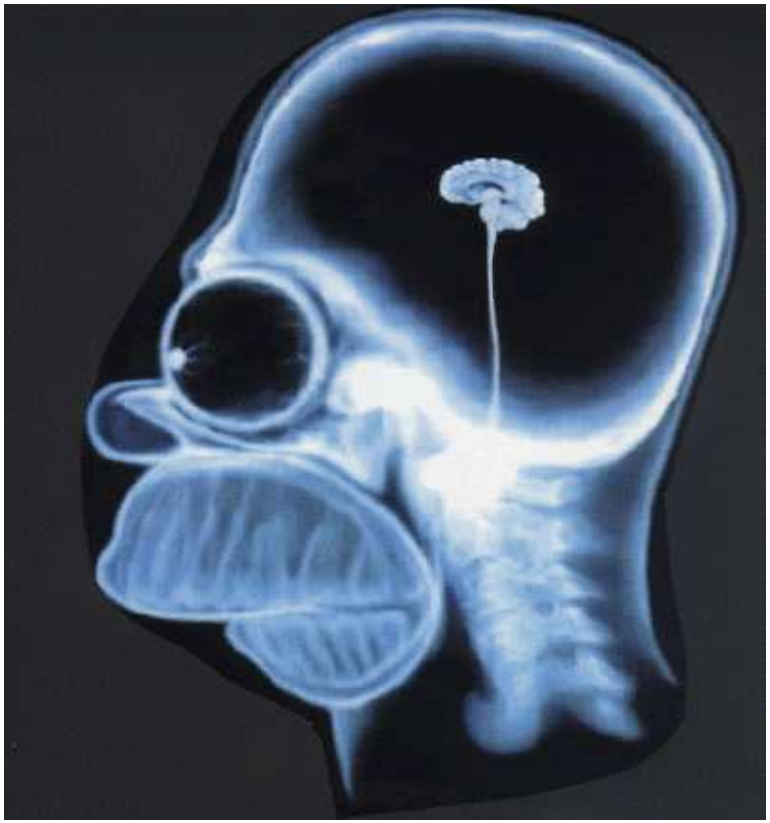
Warnings

1. All cases are true cases
2. Some may not be infectious encephalitis
3. Focus on cases where ‘something had to be done’



Warnings

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-marketting’
- 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

Case 0. Learning point (2)

Drug-Induced Aseptic Meningitis

Four main class 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° = 38°C
- Nuchal rigidity
- Oriented, no deficit

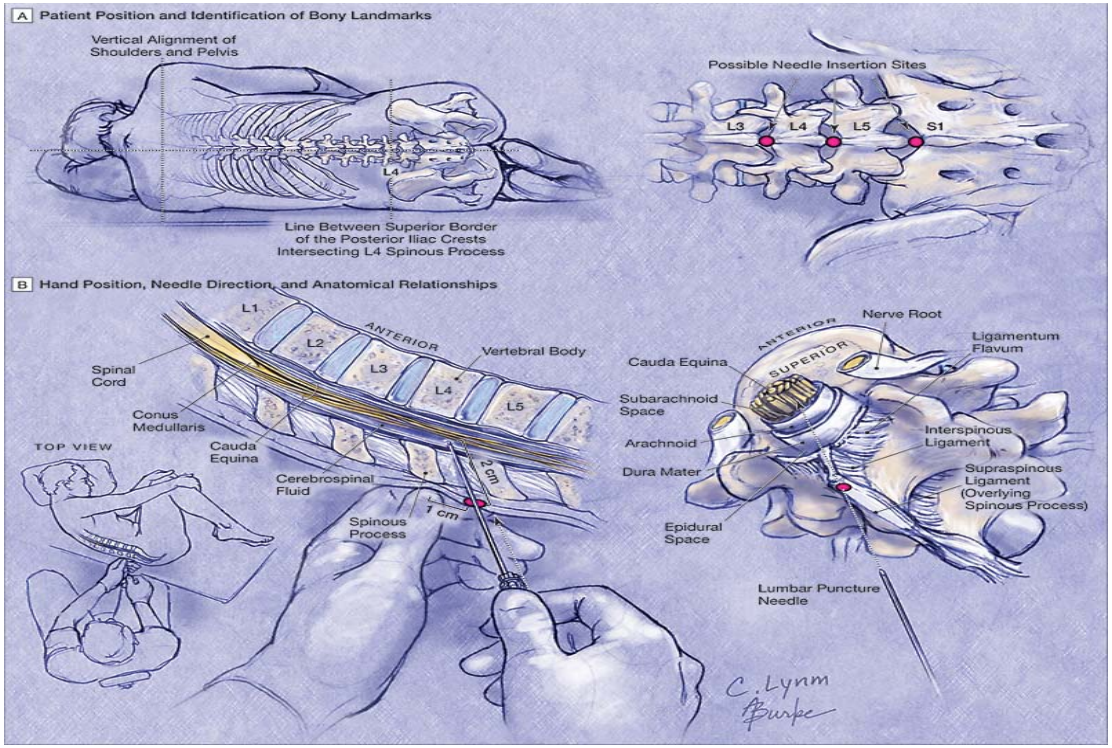
A strange bank boss (2)

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 ?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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

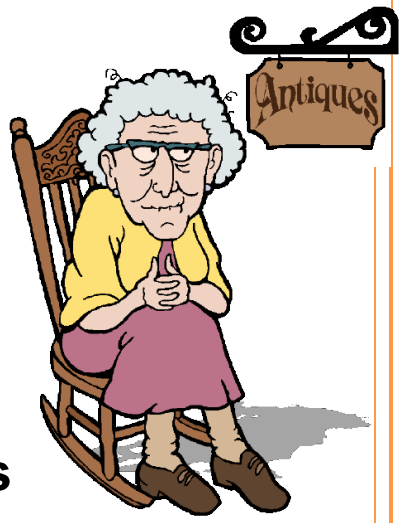
2. Meningitis and encephalitis very close

- 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° = 39°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

1. What do you suspect ?

2. Additional investigation(s) ?

3. Empirical treatment ?

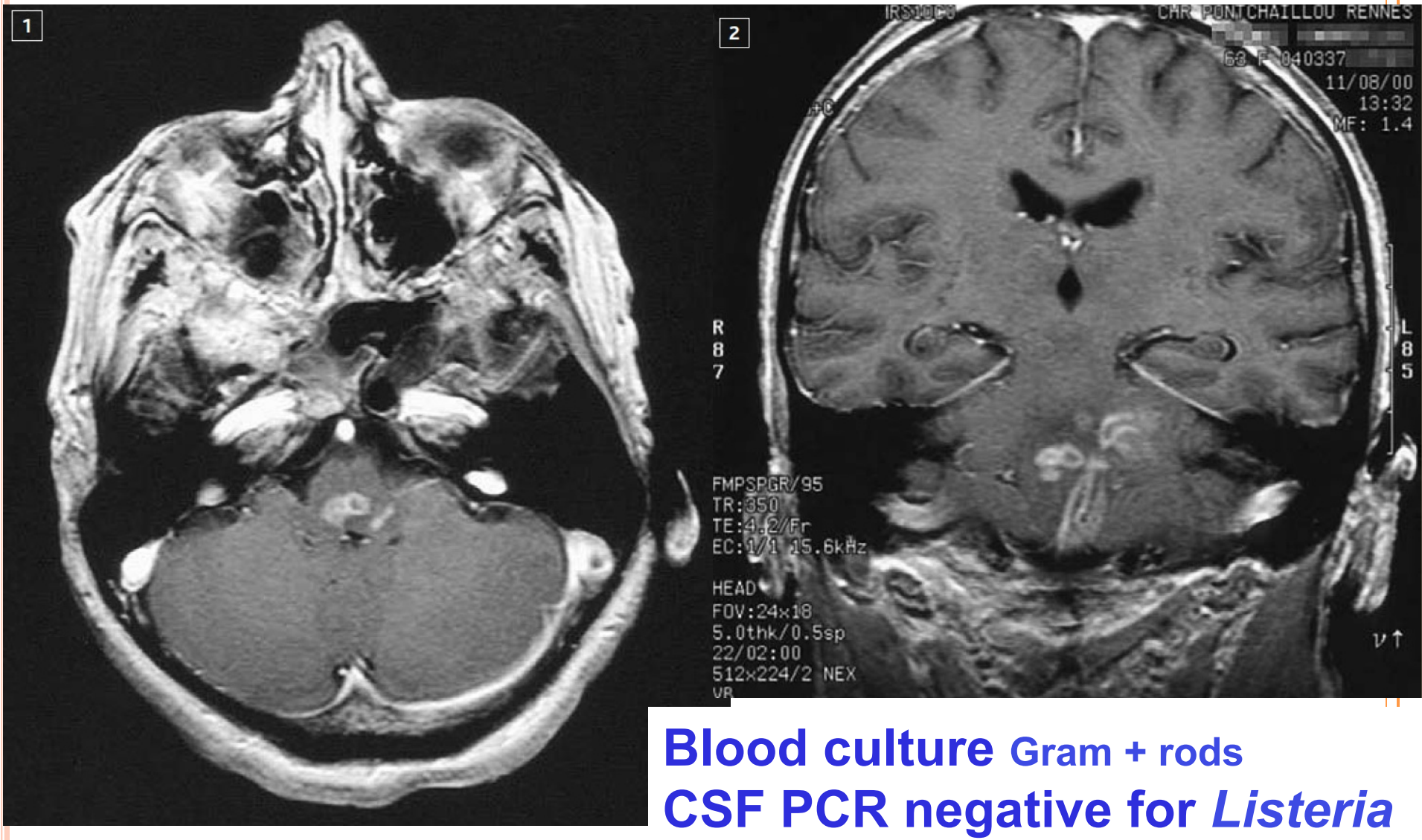
Biochemistry

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

Bacteriology negative (direct examination)

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

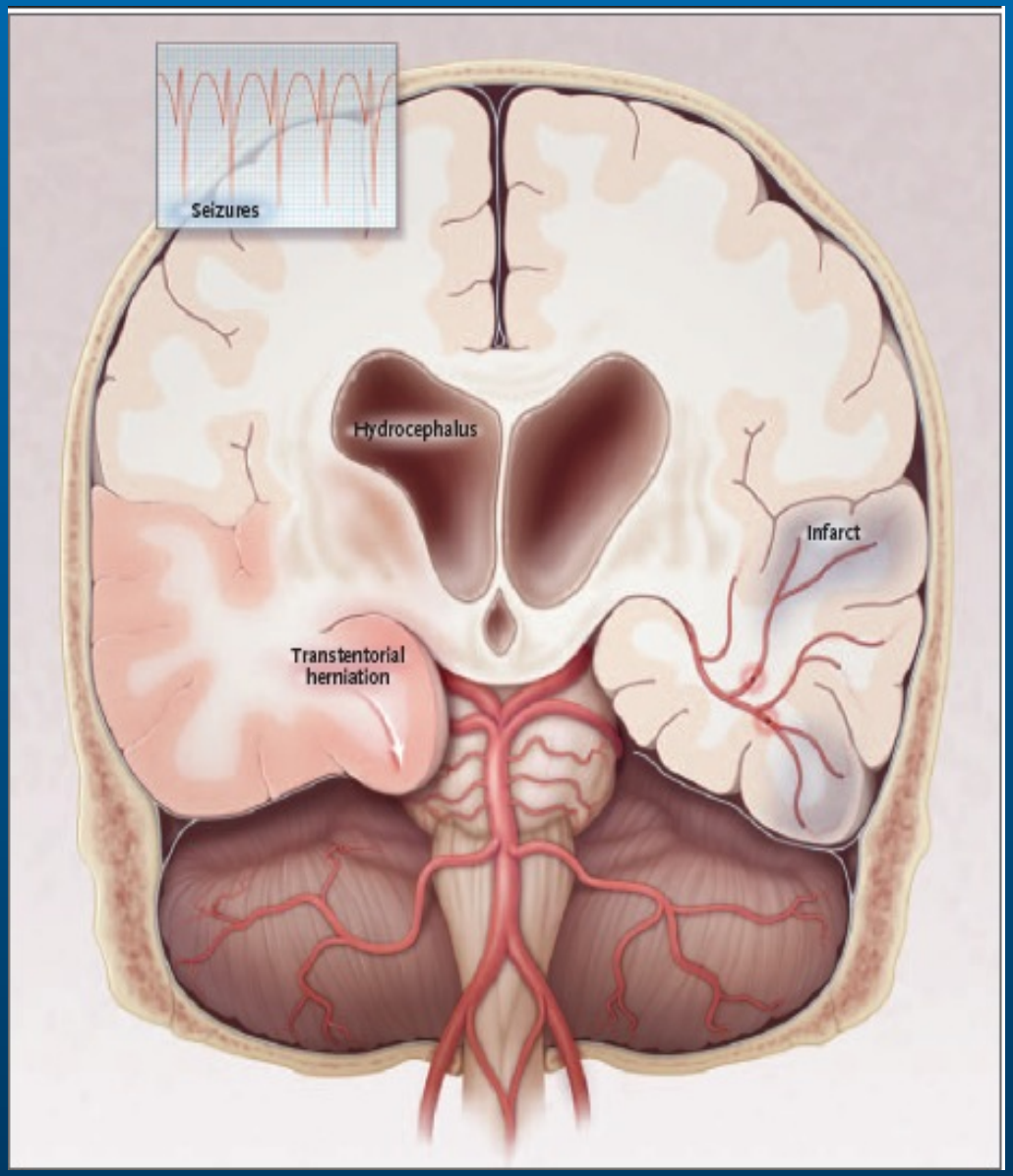
Admission

- Body T° = 39°C
- Blood pressure 110/70 mmHg
- Not sedated, GCS = 6
- Rash


3/2

What do you do, **right now ?**

CT scan before LP ?



COMPUTED TOMOGRAPHY OF THE HEAD BEFORE LUMBAR PUNCTURE IN ADULTS WITH SUSPECTED MENINGITIS

RODRIGO HASBUN, M.D., JAMES ABRAHAMS, M.D., JAMES JEKEL, M.D., AND VINCENT J. QUAGLIARELLO, M.D.

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

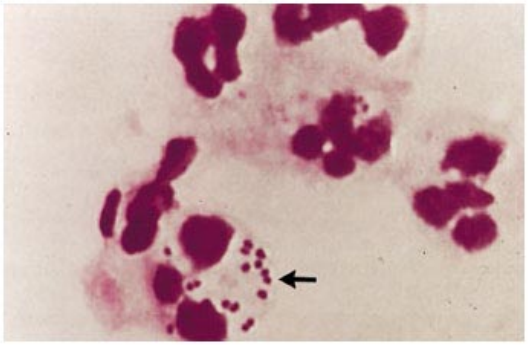
- Blood cultures (twice within 10 minutes)
- Skin biopsy (culture, PCR)

Imaging

- CT scan or MRI (whatever is available first)

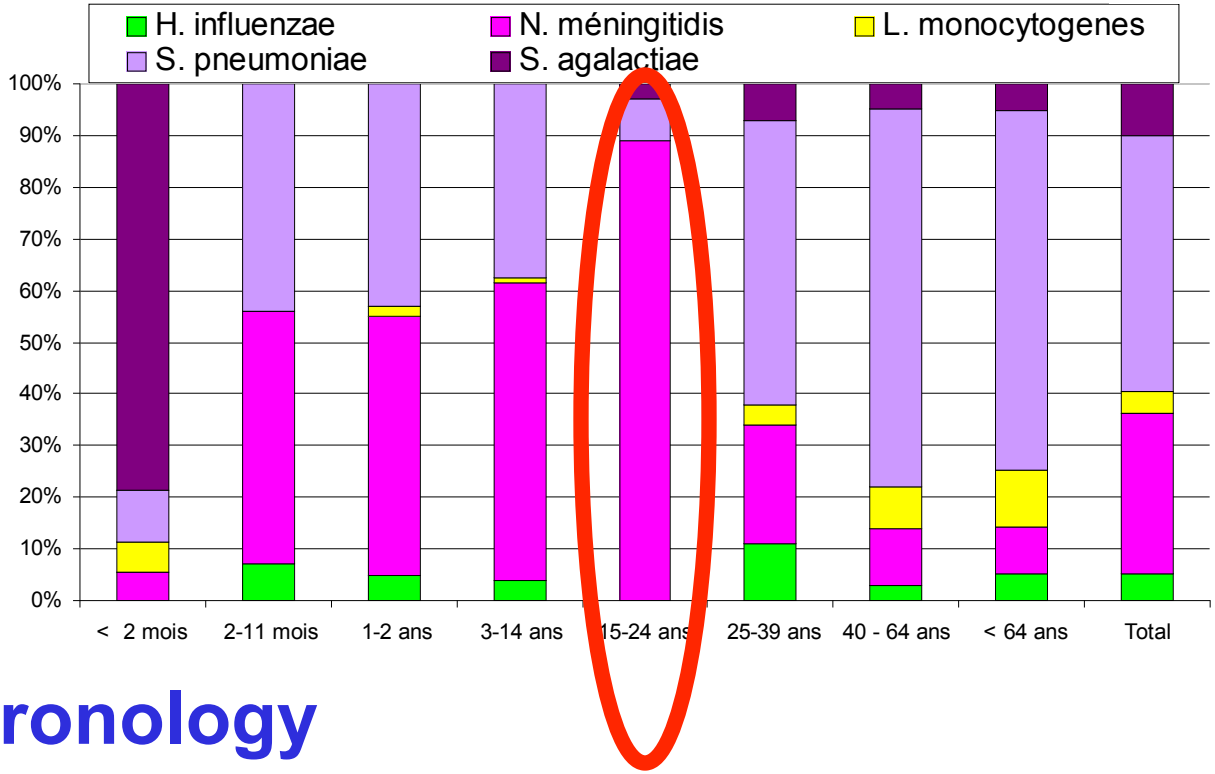

Noncontrast CT

Final diag: Meningococcal meningitis



1. Host

- Young (< 25 years), no comorbidities



2. Chronology

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

3. Purpura

ORIGINAL ARTICLE

Clinical Features and Prognostic Factors in Adults with Bacterial Meningitis

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°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°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°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)

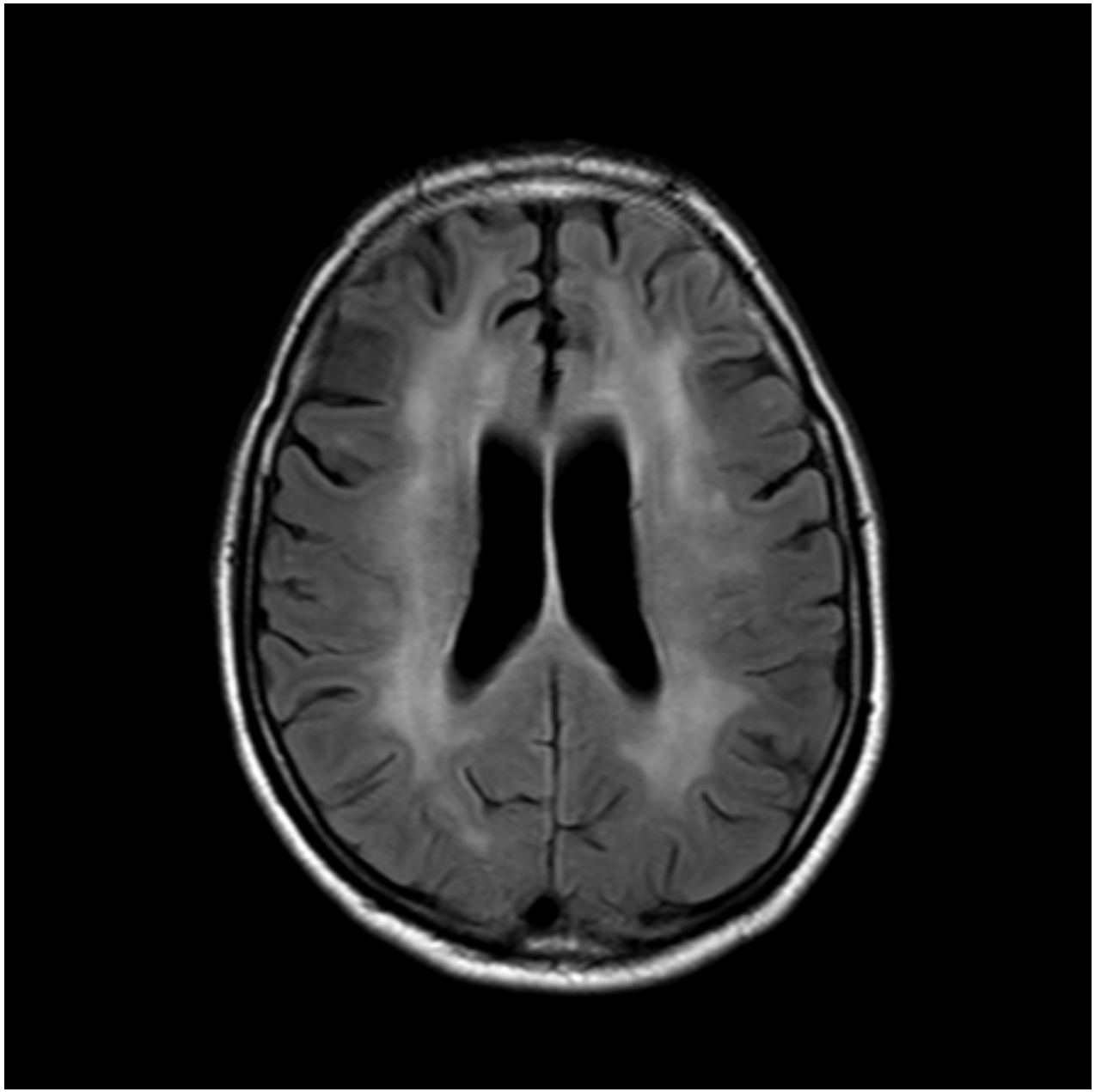
Bacteriology negative (direct examination)

1. What do you suspect?

2. Additional investigation(s) ?

3. Empirical treatment ?

Brain MRI



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

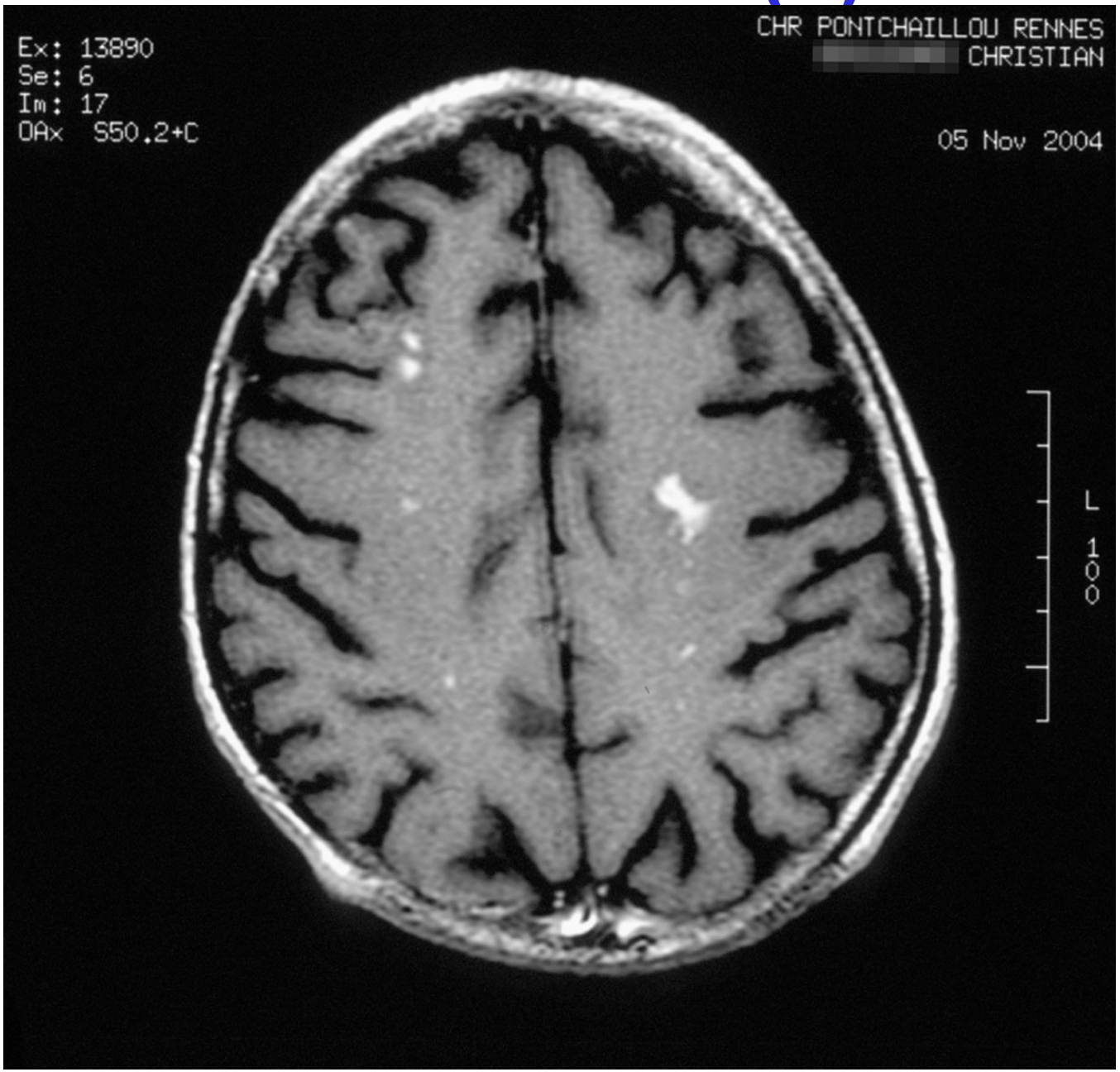
- Severe seronegative rheumatoid arthritis (10 years)
- Stabilized with prednisone, 50 mg/day (5 years)
- Progressive weight loss (- 20 kg in last 2 years)
- Chronic diarrhea (1 year)
- Dyspnea (6 months) -> severe mitral regurgitation (3/4)

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)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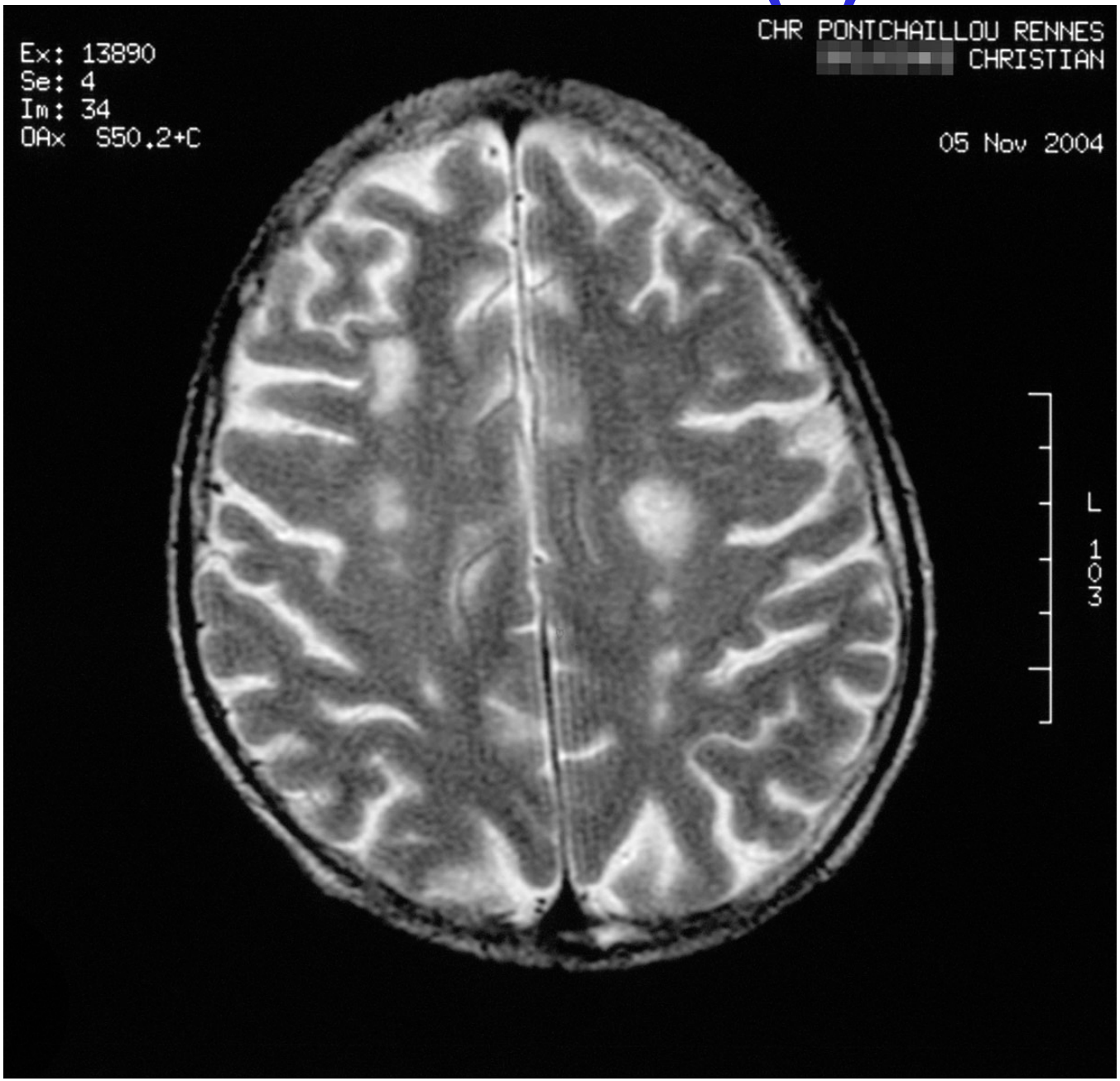
Brain MRI (2)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Case 6 – When everything goes wrong

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 whipplei* +

Dramatic improvement (including brain MRI), with

- One month ceftriaxone
- One year cotrimoxazole

Excised mitral valve

- PCR ARN 16S: *Tropheryma whipplei* +

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

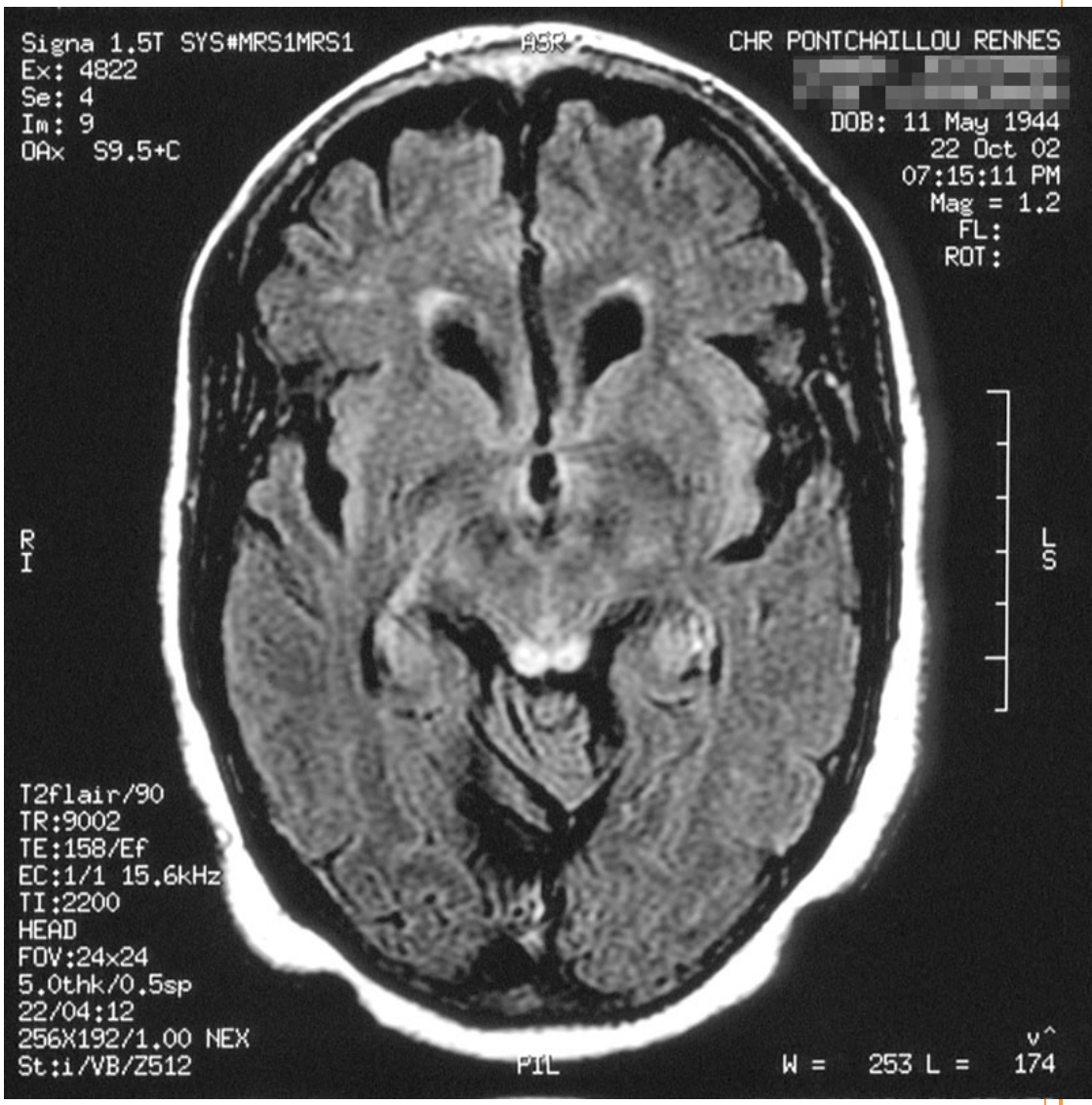
Secondary

Altered mental status

Ophtalmoplegia, nystagmus

Severe memory disorders

CSF ‘normal’ (prot 0.5 g/L)



Thank you !