Case Presentation

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Diagnosis Dilemma

- 65 female
- Recent discharge (moved to homeward) – on 26/8 – Stroke (acute thalamic infarct) , PE – started apixaban, LRTI.
- Mobility was improving now requiring minimal supervision only
- BG- Epilepsy – well controlled, Learning Disability . I mobile at home
- Normally independent with ADLS

- On 24/9 due to increasing confusion moved to acute ward – bloods normal, mildly tachycardic . IMP- post stroke cognitive impairment.
- On 25/9 – seizures and raised temp. Had 14 seizures , lasting 2-3 min , GTC . Bloods mild AKI , CRP – normal , CXR- NAD .
- Phenytoin loaded , Started aciclovir and ceftriaxone on 25/9 . Later loaded with Keppra as well

- Discussed with neurology on 25/9 – MRI head , LP and EEG .
- MRI-on 19/8 - Acute left thalamic infarct
- MRI- on 28/9- Complete resolution of the changes in the left thalamus and cortical changes in the left cerebral hemisphere. The previous appearances were not entirely typical of ischaemia , especially the cortical changes. Could this have represented form of encephalitis? Advise discussion in the neuroradiology MDT in QE.

- EEG – on 30/9- consistent with seizure activity , D/D encephalitis or CJD.
- LP on 29/9 – NAD , viral PCR – negative
- Auto immune encephalitic syndrome screen – negative
- Discussed with Edinburgh labs – unlikely CJD .

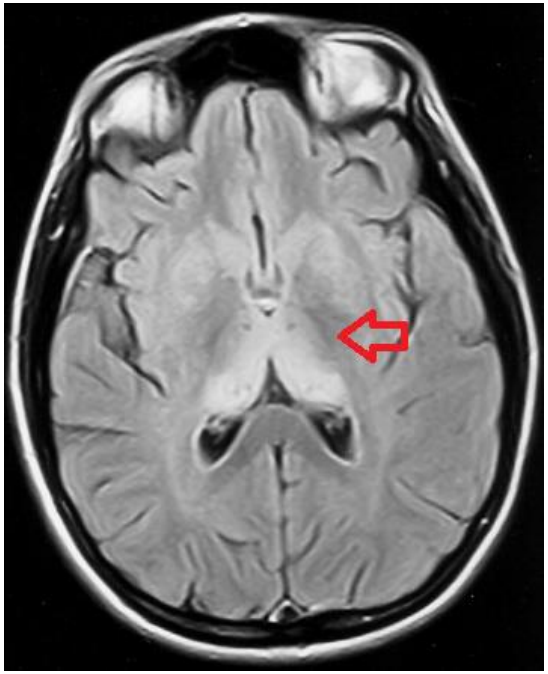
- Later on 01/10/20 – noticed to have further seizure activity lasting few seconds , GTC – then noticed to have RT side weakness .
- Was discussed with Stroke Consultant and patient reviewed by them –
- IMP- ? Further stroke/ ? Encephalitis/ ? Todd's palsy
- For Transfer to stroke ward and repeat MRI DWI

- MRI- 02/10/20- Limited MRI study shows new left parieto-occipital abnormal cortical restricted diffusion , may be ischaemic/encephalitis for further MDT neurology discussion.
- Addendum by neuroradiologist (05/10/20)-The distribution of changes seen on the diffusion weighted sequence crosses vascular boundaries therefore not ischaemic. This is likely related to patient's seizure. Choroid plexus appearances is within normal limits.

Please consider CSF evaluation to assess for other causes such as encephalitis.

- Continued Aciclovir and already on apixaban , for stroke rehab.
- Discussed with neurology again on 07/10- advised- Encephalitis post stroke ? Viral and seizures due to encephalitis. No further neurology input needed
- Rehab continued and completed 2 weeks of aciclovir. Was also on NG feed during this time

- On 25/10 – Multiple seizures – again discussed with neurology – increased dose of valproate and previous MRIs reviewed – suggested hockey stick sign in thalamus ? CJD.
- Advised repeat MRI with contrast – on 28/10-Suboptimal scan showing: - No acute intracranial pathology or restricted diffusion detected. - No definite abnormal enhancement identified after IV contrast administration.



- Did not have further seizures – so discharge planning continued with new baseline of Hoist onto stroke chair.
- Awaiting repeat EEG .

- Most likely diagnosis – Encephalitis (? Viral/ Post Stroke) . Seizures secondary to encephalitis/stroke on BG of epilepsy

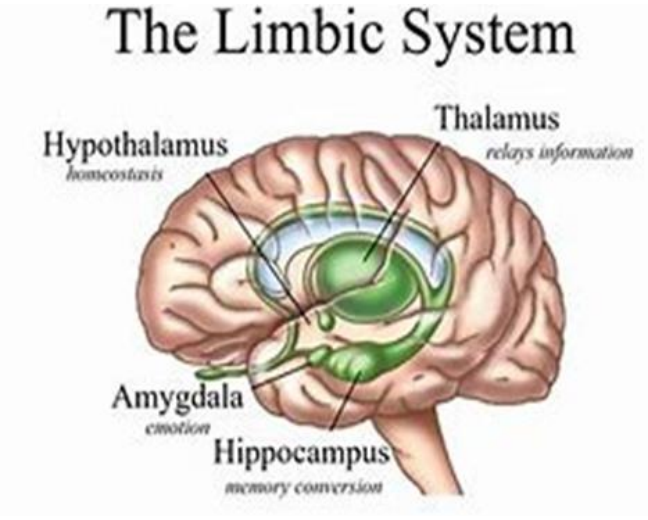
Encephalitis

Encephalitis

- Inflammation of the brain parenchyma secondary to direct infection, post-infectious or none infectious immune response.
- Estimated incidence 5500 cases in UK/year
- Can be localised e.g. limbic/brainstem or widespread.

Limbic system

- Hypothalamus – regulates hormones, homeostasis, ANS, regulates behaviour & emotional responses
- Amygdala – emotional responses & motivation
- Hippocampus – learning and memory



Presentation – limbic encephalitis

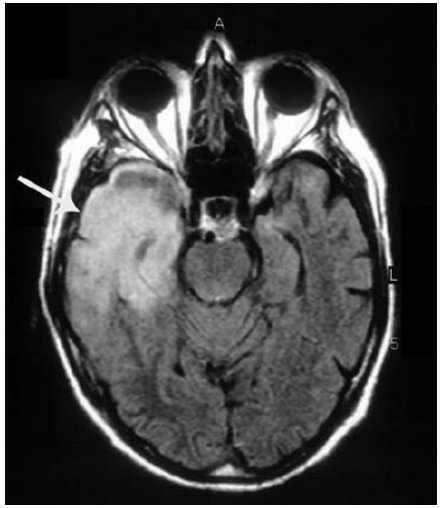
- Subacute (days-weeks, most few months)
- Cognitive, esp memory impairment (anterograde)
- Seizures (complex partial + secondary generalised, temporal lobe)
- Personality change + psychiatric symptoms
- Hallucinations
- Alterations in consciousness
- Viral – flu like prodrome, headache

Presentation – Brainstem encephalitis

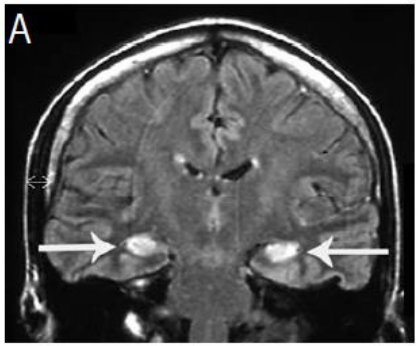
- Lower cranial nerve involvement
- Myoclonus
- ANS dysfunction
- Locked in syndrome
- Respiratory disturbance
- Ophthalmoplegia
- Disturbance in consciousness
- Ataxia

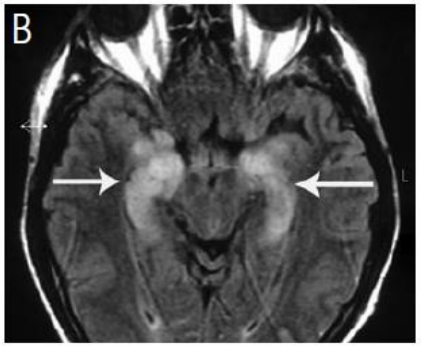
Infective

- **herpes simplex type 1** - most common
- Immunocompromised; herpes simplex type 2, and human herpes viruses (HHV) 6 and 7
- HSV;
  - abrupt onset, fever common
  - Signal change + swelling temporal lobes – MRI
  - CSF; lymphocytosis, ↑protein, PCR
  - Mortality 70% untreated
  - IV aciclovir reduces mortality to 20-30%

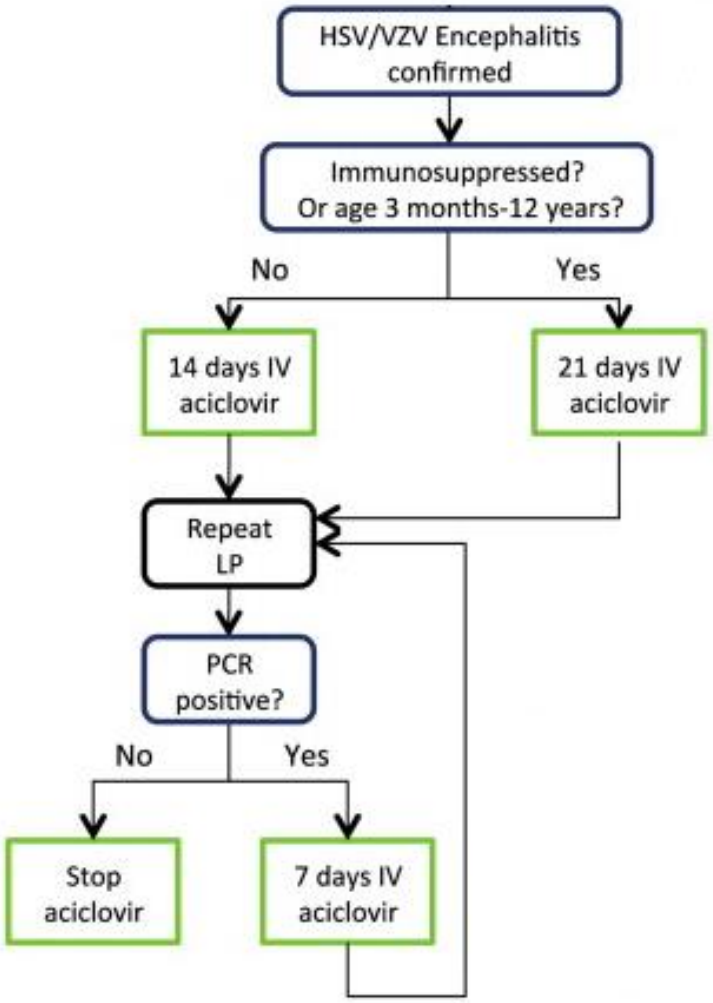


- HHV;
  - Hippocampal changes on MRI
  - ganciclovir +/ foscarnet





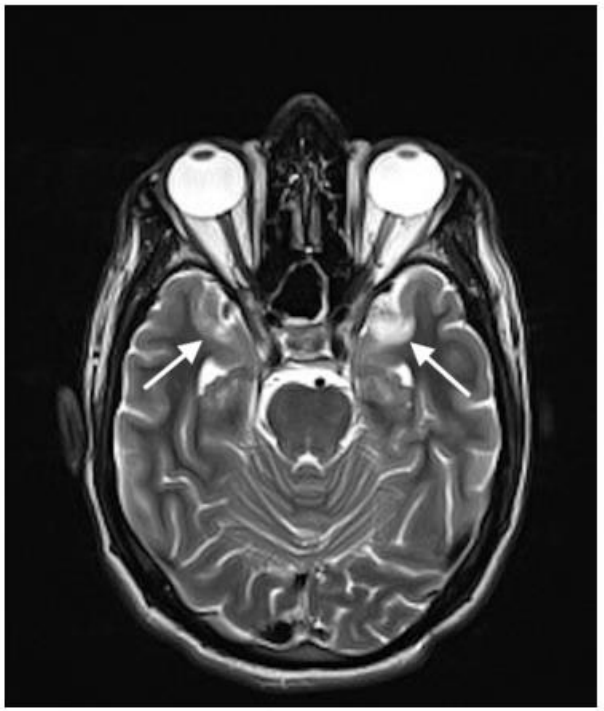
HSV encephalitis



Association of British Neurologists and British Infection Association National Guidelines

Infective

- Other viruses; VZV, EBV, CMV, MMR, Japanese B, rabies, poliovirus, adenovirus, influenza
- Bacterial e.g. Neurosyphilis, T.B, Lyme, listeria
- Fungal
- parasitic
- Creutzfeldt–Jakob disease
- Case reports of SARS-CoV-2



Autoimmune Encephalitis

- Inflammation 2^{o} to an immune response.
- Subdivided into to 2 groups depending on whether they are related to malignancy
- Acute or more commonly subacute presentation

Paraneoplastic Encephalitis

- Perivascular lymphocytic infiltration, neuronal cell loss, and reactive microglial proliferation
- Immune response
- Most common cancers; lung, thymus, ovary, breast or testes
- Associated with onconeural abs, but not detected in 40% of ppl

Paraneoplastic antibodies

Antibody	Associated tumour
Anti-Hu	Bronchial small cell carcinoma
Anti- Ma2 (Anti-Ta)	Testicular tumour
CRMP5/CV2	Lymphoma, small cell lung cancer
ANNA-3	Bronchial small cell carcinoma

Paraneoplastic encephalitis

- Not all pts have changes on MRI
- Precedes cancer Δ in 60% by average 3.5 months
- When tumour detected no local/distant spread in 75% cases
- Investigations; CT TAP, mammogram/testicular uss + tumour markers or FDG-PET

Non-paraneoplastic autoimmune encephalitis

Subdivided according to autoantibodies

- **VGKC** associated proteins **LGI1** & **CASPR2** abs - previously known as VGKC
- **NMDA abs**
- **AMPAR abs**
- **GABAB/AR abs**

**Brain imaging + LP can be normal

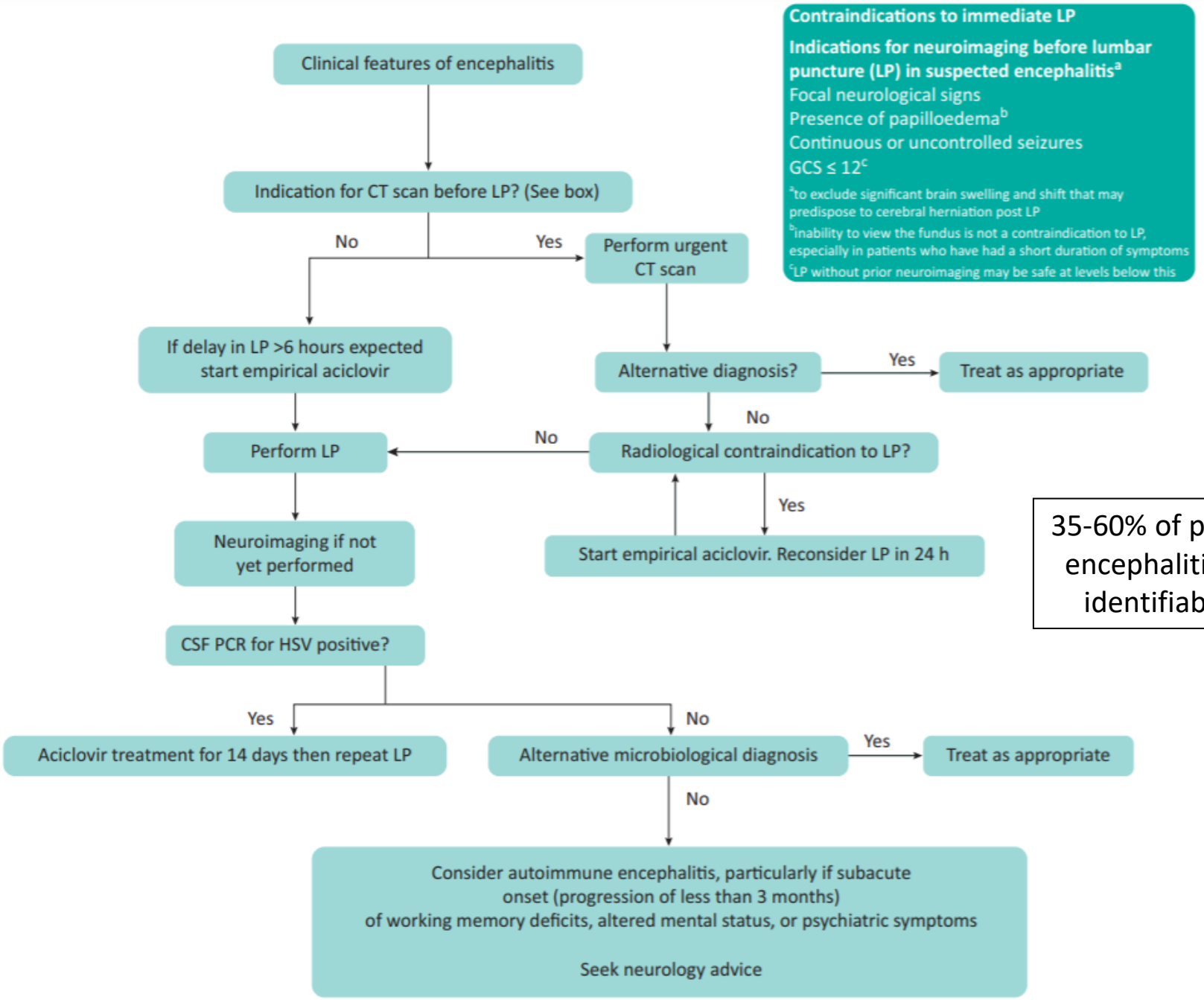
VGKC

Voltage gated potassium channels (VGKC); membrane bound proteins responsible for repolarising the nerve terminal after the passage of each AP. Widely expressed in limbic system.

- Middle age
- More common in men
- Fever + headache uncommon
- Seizures common, hard to control, faciobrachial dystonic seizures
- ↓Na+ 2^{o} SIADH
- REM sleep disorder
- MRI; 60% ↑ signal hippocampus
- EEG; diffuse slowing/focal, usually temporal lobe sharp waves
- CSF none specific, oligocloncal bands, LGI1/Caspr2 abs
- Serum VGKC protein associated abs (LGI1/Caspr2)
- Rx; plasma exchange, intravenous immunoglobulin (IVIg), and high dose oral steroids

N-methyl-D-aspartate receptor abs

- Young women
- Ovarian teratoma, 70% are benign
- prodromal flu-like illness, headache
- severe psychiatric symptoms; Agitation, periods of staring, dystonia and catatonic posturing
- MRI often normal
- NMDA abs in serum/CSF
- Rx; tumour resection + immunosuppression



35-60% of people with encephalitis have no identifiable cause

Fig 1. Algorithm for basic management of acute encephalitis (based on UK guidelines).[6] CSF = cerebrospinal fluid; GCS = Glasgow Coma Scale; HSV = herpes simplex virus; LP = lumbar puncture; VZV = varicella zoster virus

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