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## The management of infants and children treated with aciclovir for suspected viral encephalitis.

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## **ABSTRACT**

### **Objective**

To investigate how infants and children with suspected viral encephalitis are currently managed in a UK tertiary children's hospital.

### **Methods**

Case note review of all infants and children who received intravenous aciclovir for suspected encephalitis over a six month period.

Suspected viral encephalitis was defined as a child with fever or history of febrile illness and a reduced level of consciousness, irritability or a change in personality or behaviour or focal neurological signs.

### **Results**

Fifty-one children were identified. Two had proven herpes simplex encephalitis (HSV) and two had clinically diagnosed viral encephalitis with no cause identified. Forty children had cerebrospinal fluid analysis, but basic results were incomplete in 13 cases.

Cerebrospinal fluid was sent for the detection of HSV DNA by polymerase chain reaction in 27 cases. The initial dose of aciclovir was incorrect in 38 cases. The median (range) length of intravenous aciclovir treatment was 4 (1- 21) days. Six children were given a full course of aciclovir (10 or more days). For 14 children, there appeared to be no real indication for starting aciclovir. Case note documentation was generally inadequate.

### **Conclusions**

The management of children with suspected viral encephalitis appears haphazard in many cases. Guidelines for the management of children with suspected viral encephalitis are needed.

## **INTRODUCTION**

Fever, seizures, irritability or reduced level of consciousness are common childhood symptoms and signs. Children with these features may have a central nervous system (CNS) infection including viral encephalitis. The commonest diagnosed cause of encephalitis in the United Kingdom (UK) is herpes simplex virus (HSV) type 1<sup>1</sup>.

Untreated, the mortality of HSV encephalitis is approximately 70%. This can be reduced significantly to 20% if intravenous (IV) aciclovir is given<sup>2,3</sup>. Because it usually takes several days to confirm the diagnosis, aciclovir treatment is started if there is a strong suspicion

of HSV encephalitis; this will usually be based on appropriate clinical features and cerebrospinal fluid (CSF) or imaging findings consistent with viral encephalitis<sup>4</sup>. Earlier treatment is associated with a better outcome<sup>5</sup>. However initiating treatment too early, without appropriate investigations, or in patients for whom there is no clear indication, can make the subsequent management difficult. The standard treatment for HSV encephalitis is now 14 to 21 days of intravenous aciclovir, because of apparent relapses following shorter courses<sup>6-8</sup>. But maintaining this treatment course in patients in whom it was never proven whether or not they had HSV encephalitis is difficult, leading to tough decisions about when to stop the treatment<sup>4</sup>. The aims of this study were to investigate how children admitted with suspected encephalitis were managed, by looking at their investigations and treatment.

## **METHODS**

The study was conducted at the Alder Hey Children's NHS Foundation Trust, a large secondary and tertiary paediatric centre serving a population of approximately 3.5 million people, with more than 60,000 new attendances to the emergency department every year. We retrospectively studied all children admitted over a 6 month period (February - November 2005) who were treated for suspected viral encephalitis. To identify such children we obtained from pharmacy records all children prescribed IV aciclovir; after reviewing the case notes we excluded those who had localised skin infections or immunocompromised patients (mainly oncology cases) treated for cutaneous varicella zoster (chicken pox) infection. Details of the presenting clinical features, and the relevant investigations and treatments were obtained from the case notes.

Children were considered to have "suspected viral encephalitis" (and therefore have an indication for treatment with IV aciclovir) if they had a fever or history of febrile illness and a reduced level of consciousness, irritability or a change in personality or behaviour or focal neurological signs<sup>9</sup>. Children were subsequently classified as having a diagnosis of "proven viral encephalitis" if a viral cause was identified, or "clinically diagnosed encephalitis" if their clinical picture, cerebrospinal fluid (CSF) findings and other investigations were consistent with viral encephalitis, but no virus was identified. The initial management of children with seizures or a febrile illness or both

was assessed for whether NICE guidelines were followed<sup>10 11</sup>. We considered the dose of IV aciclovir given to be correct if it agreed with the doses quoted in the British National Formulary for Children: 20mg/kg tds for infants aged 1 to 3 months; 500mg/m<sup>2</sup> for children aged 3 months to 12 years; 10mg/kg tds for children over 12 years or over. The study was registered with the Trust audit department and all data were handled according to national guidance.

## RESULTS

### Clinical features

56 children receiving IV aciclovir were identified of whom 51 were included (5 had received the drug for other indications). Twenty-five (49%) children were admitted via the emergency department and 26 (51%) were transferred to the intensive care department from local district general hospitals.

The clinical features at presentation are summarised in table 1, and initial diagnoses, investigations, results and final diagnoses are given for each patient in table 2. One child was immunocompromised through treatment for acute lymphoblastic leukaemia. Thirty-one children had a history of seizures, or had witnessed seizures (19 generalized tonic-clonic, 12 complex partial). Fourteen children had new focal neurological signs; 4 with increased tone and reflexes, 4 with pupil abnormalities, 2 with facial weakness, 2 with abnormal posturing, 1 with dysarthric speech, and 1 with a lateral rectus palsy. Documentation of symptoms and signs was inadequate in many cases (table 1), for example only two thirds had the presence or absence of a rash noted, less than two thirds had a coma score recorded, and only one half had presence or absence of neck stiffness documented. Thirty-seven children (72%) met the case definition for suspected viral encephalitis, or had aciclovir started in accordance with the NICE febrile illness guidelines. But for 14 children there appeared to be little rationale for starting aciclovir. Initial diagnoses in these children included: new onset afebrile seizure(s) in 4 children, sepsis/meningitis in infants less than 3 months (4 children), afebrile status epilepticus in children with epilepsy and a pre-existing severe neurological disorder (2 children), acute cerebellitis (1 child), malfunction of a ventriculo-peritoneal

shunt (VP) (1 child), afebrile seizures following head injury (1 child), deliberate drug overdose (1 child).

### Investigations

Seventeen children had a LP and two had CSF sampled from their VP shunt on the day of admission. Twenty had an LP subsequently and one had CSF sampled during surgery for a temporal lobe abscess, but 11 never had a LP. The median (range) day of illness CSF was analysed was 3 (1- 21). Fifteen children had a cerebrospinal fluid (CSF) pleocytosis. CSF analysis was incomplete in 13 cases: in 3 this was because CSF protein or glucose was not sent and in 10 because no paired plasma glucose was sent. All children who had CSF analysis undertaken had bacterial culture performed; three (8%) were positive (two *Mycobacterium tuberculosis*, one *Streptococcus pneumoniae*). However, only twenty-seven (53%) children had CSF polymerase chain reaction (PCR) sent for HSV DNA (in 7 this was before aciclovir was started); one patient was PCR positive (HSV type 1). LP results confirmed the clinical diagnosis in 5 (10%) children and changed management in 31 (79%) cases, for example by allowing discontinuation of aciclovir and/or antibiotics. One neonate, with blistering lesions on the scalp, had vesicle fluid positive for HSV type 2 by tissue culture and electron microscopy and had both a CSF picture and MRI findings consistent with encephalitis, though HSV PCR was not requested on the CSF. Seven children (14%) had bacterial meningitis proven microbiologically by CSF or blood culture, and one child had a pneumococcal brain abscess.

Seven (14%) children had an EEG. All had abnormal findings: 3 had diffuse encephalopathy (patients 16, 23, 24), 3 had focal epileptic discharges (patients 13, 20, 43), and one had epileptic encephalopathy (patient 49). The EEG confirmed the diagnosis in 2 children, one with Panayiotopoulos syndrome (patient 13) and one with new onset of epilepsy (patient 20). Forty-three (84%) children had neuroimaging: 25 had computer tomography (CT), 5 had magnetic resonance imaging (MRI), 13 had CT followed by MRI. Eighteen children had abnormal findings, including four with changes of encephalitis which was felt to be consistent with HSV encephalitis for two.

## Management

In 38 children (74%), the initial dose of aciclovir prescribed was incorrect; in 20 it was sufficiently incorrect to require recalculation. Surface area was used for dose calculation in 17 of the 32 children (53%) in whom it was indicated. Renal function was tested in 47 (92%) of the children on admission. No children developed renal impairment during their admission. The median (range) length of IV aciclovir treatment was 4 (1- 21) days. Six children were given a full course of aciclovir (10 or more days). Three received 21 days aciclovir; one intravenously and two completed their course orally (after 18 and 19 days of IV treatment respectively). No children were given oral valaciclovir. The reasons for discontinuing aciclovir before 10 days were documented in 15 (29%) cases: negative HSV PCR in CSF (7 patients), rapid clinical improvement (5 patients), loss of venous access and clinical improvement or alternative diagnosis suspected (2 patients), tuberculous meningitis confirmed (1).

Antibiotics were prescribed in 50 (98%) cases: with cefotaxime given in 45 cases. The median (range) length of antibiotic treatment course was 7 (1-14) days. The only child that did not receive antibiotics had a diagnosis of acute para or post infectious cerebellitis. There were no deaths and in the children with clinically diagnosed or proven encephalitis no clinical relapses occurred.

## DISCUSSION

Viral encephalitis is an uncommon, but serious and sometimes fatal, disorder. The incidence in the UK is unknown, and there are many possible causes, but the commonest proven cause is HSV type 1, which is treatable with the intravenous antiviral drug aciclovir<sup>2</sup>. Although proven HSV encephalitis is rare, children presenting with features consistent with suspected viral encephalitis are not, and so presumptive treatment is often started. In our study, over a 6 month period 51 children were treated with aciclovir, for four of whom viral encephalitis was finally diagnosed clinically, including two with an identified viral cause – one HSV1 and one HSV2. Our study was limited by its retrospective nature, and the fact that it would have missed children with suspected encephalitis not given aciclovir, though the existence of such children seems unlikely given the readiness with which the drug appears to be given.

Nevertheless there are some clear messages from our data. For 14 (27%) of the 51 children treated with aciclovir, there was no real indication for this treatment in the first place: seven presented with a single or multiple seizure which were not associated with a febrile illness, and which are thus not an indication for aciclovir<sup>10</sup> - indeed two of these children were already known to have epilepsy, and one had an acute head injury. However of those that presented with seizures, one that subsequently developed diarrhoea ultimately proved to have a rotavirus encephalopathy, and another had a cerebral abscess, so it might be argued aciclovir treatment was justified in these patients. The other children treated with aciclovir but with no clear indication included one with a problematic ventriculo-peritoneal shunt, one who had taken a drug overdose, and four young infants with clinical features of sepsis; although antibiotics are indicated in such children, there are no guidelines or suggesting aciclovir should be used<sup>11 12</sup>. Notably investigations, including LP, were incomplete in 5 of these 14 children. Interestingly in almost all the cases where aciclovir was given without a good indication, the initial diagnosis considered by the clinician (which was not encephalitis) proved to be correct.

The results confirm our suspicion that in recent years a tendency has developed among many paediatricians to start all children who are acutely unwell and who may have a CNS infection on IV aciclovir as well as broad spectrum antibiotics, even though there is no evidence base for the aciclovir usage. The reasons for this trend are unclear, but may be because the well publicised guidelines for the management of meningococcal meningitis and septicaemia in children<sup>13</sup> have been inappropriately extended to include giving aciclovir to all children with any suspected CNS infections. Although aciclovir is generally considered to be a safe drug, serious side effects are reported including renal impairment (especially when given with ceftriaxone), hepatitis, and bone marrow failure<sup>14 15</sup>. A more common problem with the over-use of aciclovir is the decision about when to stop treatment; especially in the child who appears to be recovering, and who has not been investigated fully with LP. Prolonged treatment and the associated lengthy hospital stay adds to the economic burden on the NHS<sup>16</sup>. In most cases a complete course of aciclovir was not given, but the rationale for stopping was not explained in the notes. Given that HSV encephalitis can

occasionally relapse, the rationale for stopping the drug should be clearly documented. In some patients treatment was changed from IV to oral aciclovir, presumably because of problems with venous access. Our practice, should this be necessary, is to give at least 10 days intravenous treatment if possible, and then use oral valaciclovir, because of its better bioavailability than oral aciclovir<sup>17</sup>.

Our results suggest that in this group of children, aciclovir was given too readily without proper consideration of the most likely diagnosis and without undertaking the necessary investigations. This is in contrast to a recent report of suspected encephalitis in adults in the USA where there were inappropriate delays before starting treatment<sup>18</sup>. An earlier report from the UK suggested that guidelines would be helpful<sup>16</sup>.

Previously, we showed that only 53% of children with suspected CNS infection had a LP<sup>19</sup>. Following this, LP guidelines were published on our hospital intranet, and there has been regular teaching of junior doctors. In the current series, 37 children (72%) with suspected encephalitis had a LP which appears to indicate an improvement; however, 32 children did not have an immediate LP, though in most cases there was no contraindication to it; 20 of these had an LP subsequently, but in 11 the investigation was not performed at all. Even a week after starting treatment LP can be useful, because HSV DNA may be detectable up to this time<sup>20</sup>. Surprisingly, in our study, even when a LP was undertaken, CSF HSV PCR was not always requested, despite the child being treated for suspected HSV encephalitis. If encephalitis is suspected strongly enough on clinical grounds and CSF analysis findings and a decision is made to start aciclovir then HSV PCR should always be requested on the CSF.

If the initial CSF results are normal, the diagnosis of a CNS infection (and in particular encephalitis) is unlikely and it is possible that a decision to start aciclovir could be considered but deferred as long as the child continues to be observed in hospital. Although HSV encephalitis has occasionally been reported in patients without a CSF pleocytosis, this is rare, and tends to occur on only the first day or two of illness, with a repeat LP usually revealing cells<sup>21 22</sup>. This does not appear to be current practice: we found that 18 of the 40 children that had CSF analysis had a normal CSF, and therefore may not have

needed aciclovir treatment at all, if the treatment had been guided by the CSF findings. For these children, a prolonged course of iv aciclovir seems unnecessary. We would recommend treating all children in whom encephalitis is a strong clinical possibility with iv aciclovir even if the initial CSF HSV PCR is negative for a minimum of 10 days. In this situation, the LP should be repeated and CSF HSV PCR sent again. However, if the child has made a full clinical recovery and CSF analysis and brain imaging are normal or if a definite alternative diagnosis has been reached, then aciclovir can be discontinued providing a clear rationale has been documented in the case notes. If the child subsequently shows any sign of a possible relapse, then appropriate investigations should be repeated including a LP and brain imaging and treatment restarted.

## **CONCLUSIONS**

We have shown that the management of children with suspected encephalitis appears to be haphazard. In almost a third of patients, aciclovir was started without a rationale basis and the decision to start treatment was frequently made without using appropriate investigations. Even when lumbar punctures are performed, HSV PCR is not always requested. Aciclovir is often given at the wrong dosage, and the drug subsequently stopped without explanation. Guidelines on the initial management of suspected encephalitis in children are needed.

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## **Competing interests:**

None declared.

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## **What is already known on this topic**

Children with proven herpes simplex encephalitis or clinically diagnosed viral encephalitis require at least 10 days treatment with intravenous aciclovir.

The results from cerebrospinal fluid analysis are very helpful in the management of children with suspected central nervous system infection including viral encephalitis.

**What this study adds**

Children with suspected viral encephalitis are often inadequately investigated and managed.

Guidelines for the management of children with suspected viral encephalitis are needed.

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**TABLES****Table 1** Clinical features in 51 infants and children treated for suspected viral encephalitis

<b>Clinical feature</b>	<b>Number (%)</b>	<b>Number with data recorded in case notes</b>
Age [mean (range)]	2 years (2 days to 14 years)	51
Male	28 (55)	51
Pre-existing neurological disorder	9* (18)	51
Days ill [median (range)]	2 (1-21)	51
Confusion, irritability or behavioural change	35 (76)	46
Fever (history or documented)	34 (67)	51
Seizures, history or witnessed	31 (61)	51
Vomiting	23 (57)	40
Headache	10 (47)	21
Photophobia	0	32
Glasgow Coma Score, median (range)	13 (3-15)	31
Glasgow coma score <14	21 (41)	31
Rash	9 (26)	34
Prolonged capillary time (>2 sec)	7 (18)	39
Bulging fontanelle	2 (9)	21
Neck stiffness	2 (7)	26
New onset of focal neurological signs	14 (37)	38

\* Epilepsy 4 (2 with developmental delay), cerebral palsy 2, hydrocephalus 2



**Table 2** Details of 51 children treated for possible viral encephalitis (VE) with aciclovir. Those with 'suspected VE' (see methods section) listed first

Patient number. [Age in days (D), months (M) or years (Y)]	Most likely diagnosis considered by admitting clinician	Laboratory investigations (PCR results in next column) CSF WCC (differential as percentage [%] or count) & RCC x10 <sup>6</sup> /l; CSF protein (P) g/l, CSF glucose (G) mmol/l, Glucose ratio (GR); Other investigations (if performed).	PCR results (Results from CSF unless stated otherwise)	Neuroimaging	Final diagnosis
<b>Met case definition of suspected viral encephalitis on admission</b>					
1) 9D	Staphylococcal sepsis	WCC 47 (L 66%, N 21%, M 13%); RCC 0; P 0.8, G ND; Scalp vesicle fluid HSV type 2 pos (tissue culture & direct detection)	HSV PCR ND	CT & MRI - temporal lobe abnormalities consistent with HSV VE	HSV type 2 VE
2) 13Y	URTI	WCC 542 (M 96%, N 4%); RCC 0; P 0.46, G 2.7, GR NR	HSV PCR pos type 1	CT & MRI - changes in left temporal lobe suggestive of HSV VE	HSV type 1 VE
3) 14Y	BM or VE	WCC 23 (M 17, N 4, DC 2); RCC 0; P 0.71, G 3.4, GR 0.6	HSV PCR neg	CT & MRI - N	Clinically diagnosed VE
4) 2Y	Herpes stomatitis	WCC 10 (M 9, N 1); RCC 0; P 0.3, G 2.9, GR 0.42	HSV PCR neg	CT - non specific changes in the frontal & temporal lobes; MRI - high signal in basal ganglia, thalami, external capsule and insular white matter	Clinically diagnosed VE
5) 22D	Neonatal sepsis	WCC 2; RCC 10; P 1.63, G NS	HSV PCR neg, Pneumo & Meningo neg	CT - N	Neonatal sepsis - no cause found
6) 4M	Intussusception or BM	WCC 55 (M 90%, N 10%); RCC 0; P 1.2, G 2.5, GR 0.46; BC Pneumo pos	HSV PCR neg, Pneumo pos	CT- frontal subdural collection	Pneumococcal BM
7) 11M	BM	WCC 946 (N 62%, M 30%, DC 8 %); RCC 5; P 0.98, G 2.3, GR NR	HSV PCR ND, Pneumo PCR pos; Serum PCR Pneumo pos	ND	Pneumococcal BM
8) 2.5Y	BM or VE	WCC 2080 (DC 91%, M 7%, N 2%); RCC 0; P 0.72, G 2.3, GR 0.42	HSV PCR ND, Pneumo PCR neg; Serum PCR Pneumo pos	CT - N	Pneumococcal BM
9) 6M	BM or VE	LP ND; BC Pneumo pos	LP ND	CT - signal abnormality in basal ganglia & internal capsule	Pneumococcal BM
10) 14.5Y	BM or VE	WCC 4500 (N 80%, M 10%, DC 10%); RCC 0; P 2.61, G 3.5, GR NR	HSV PCR neg, Group B Meningo PCR pos	CT - N	Meningococcal (group B) BM
11) 11M	BM	WCC 5; RCC 224; P 0.26, G 2.6, GR NR; CSF culture TB pos	HSV PCR neg	CT- communicating hydrocephalus & signs of raised intracranial pressure	TB meningitis
12) 11M	BM or VE	WCC 12 (M 10, DC 2); RCC 2; P 1.05, G 0.5, GR 0.16; CSF culture TB pos	HSV PCR neg	CT - obstructive hydrocephalus.	TB meningitis
13) 8Y	VE	WCC 13 (M 8, L 5); RCC 220; P 0.21, G 2.8, GR 0.68	HSV PCR neg	CT & MRI - N	Panyayiopoulos syndrome
14) 4Y	BM or VE	WCC 22 (N 64%, M 36%); P 0.37, G 2.4, GR 0.36	HSV PCR neg	CT- N. MRI - abnormalities in basal ganglia & white matter	ADEM
15) 1.5Y	BM or VE	WCC 26 (L 18, N 8); RCC 0; P 0.41, G 2.3, GR 0.88	HSV PCR neg	MRI - diffuse abnormalities in white matter	ADEM
16) 9M	Neurodegenerative disorder	WCC 0; RCC 2; P 0.5, G 3.6, GR ND	HSV PCR ND	MRI - abnormal signal in the basal ganglia	Undiagnosed Met Enceph
17) 2.8Y	Afebrile SE. Child with EP	WCC 0; RCC 1; P 0.11, G 5.9, GR ND	HSV PCR ND	ND	SE in child with EP

18) 15M	Partially treated BM. Child with CP & EP	LP ND	LP ND	ND	Pneumonia in Child with CP & EP
19) 3Y	BM or VE	WCC 2; RCC 0; P 0.23, G 4.2, GR ND	PCR HSV ND	CT - N	Atypical FC with pneumonia
20) 5.5Y	Sepsis or BM	LP ND	LP ND	CT & MRI - area of gliosis in frontal lobe	EP
21) 2Y 22) 5Y	Sepsis or BM Deterioration in child with Leigh Syndrome or VE	WCC 1; RCC 138; P 0.17, G 4, GR 0.81 WCC 1; RCC 0; P 0.56, G 3.8, GR 0.61	PCR HSV neg HSV PCR neg	CT - N MRI - abnormalities in thalamus, pons and cerebellar peduncles	Atypical FC Leigh syndrome (exacerbation)
23) 7Y	Met enceph or VE	WCC 1; RBC 397; P 0.44, G 4; GR 0.57	HSV PCR neg	CT & MRI - diffuse white matter encephalopathy	Leukodystrophy (exacerbation)
24) 17M 25) 28D	BM or VE Neonatal sepsis	CSF microscopy ND (bloodstained); P ND, G 3.5, GR ND WCC 0; RCC 0; P 0.31, G 2.8, GR 0.52	HSV PCR neg HSV PCR ND	CT - N CT - N	Atypical FC Neonatal sepsis - Cause unknown
26) 5Y	BM or VE in child with leukaemia	WCC 13; RCC 1; P ND, G ND, GR ND	HSV PCR ND	CT - N	Seizures with Todd's paresis
27) 6M 28) 4Y	BM or VE BM or VE	WCC 0; RCC 388; P 0.19, G 4.4, GR 0.6 LP ND	PCR HSV neg LP ND; Serum Pnemo & Meningo PCR neg	CT - N CT - N	Atypical FC Atypical FC
29) 3M	VE or atypical FC in child with CP	WCC 0; RCC 18 000; P 0.86, G 3.3, GR 0.57	PCR HSV neg	MRI - bilateral cystic encephalomalacia	EP in child with CP
30) 2.5Y 31) 2Y 32) 2M	VE VE BM or VE	WCC 0; RCC 0; P 0.18, G 3.3, GR 0.71 LP ND WCC 0; RCC 160; P 0.24, G 3.6, GR ND	HSV PCR neg LP ND HSV PCR ND; CSF Meningo, Pnemo & Entero PCR neg	CT - N CT - N ND	Atypical FC Atypical FC Viral Illness
33) 4Y	Blocked VP shunt or VE	WCC 40 (DC 100%); RCC 4160; P 0.11, G ND	HSV PCR neg	CT - shunt in situ, N sized ventricles	Focal seizures. Infected VP shunt
34) 11Y	BM or VE	WCC 0; RCC 401; P 0.21, G 4.1, GR 0.59	HSV PCR neg	CT & MRI - abnormalities in white matter consistent with ADEM	ADEM
35) 12M 36) 14Y 37) 3.5Y	BM or VE BM or VE Ophthalmic shingles & LRTI	WCC 2, RCC 3680; P 0.28, G 4.1, GR 0.68 LP ND WCC 0; RCC 0; P 0.14, G 3.3, GR 0.69	HSV PCR neg LP ND HSV PCR neg	CT & MRI -N CT - N ND	Atypical FC Atypical FC Ophthalmic shingles. LRTI

**Did not meet case definition of suspected viral encephalitis on admission / No evidence base for starting aciclovir**

38) 2Y	Afebrile seizure	LP ND	LP ND	CT - N	First seizure
39) 2M	Sepsis	WCC 5; RCC 3; P 0.58, G 2.6, GR 0.49	HSV PCR neg	CT - N	Sepsis, cause not found.
40) 2M	Sepsis	LP ND	LP ND; Serum PCR for CMV pos	ND	Cardiomyopathy; CMV pos
41) 2Y	Afebrile seizures. Diarrhoea	WCC 0; RCC 0; P 0.16, G 2.6, GR 0.92; Stool - rotavirus detected	HSV PCR neg	CT - N	Rotavirus encephalopathy
42) 10D	Neonatal sepsis	WCC 2; RCC 1810; P 0.71, G 3.9, GR 0.54	HSV PCR ND	ND	Chest infection
43) 2.5Y	VP shunt infection	WCC 17 (N 12, DC 5); RCC 2790; P 0.6, G ND	HSV PCR neg	CT & MRI no new changes	VP Shunt infection
44) 2D	Sepsis. Joint contractures & hypotonia	WCC 0; RCC 540; P 1.5, G 2.7, GR 0.77	HSV PCR ND	MRI - N	Congenital myopathy

45) 5Y	Focal seizures after head injury	LP ND	LP ND	CT - N	Head Injury
46) 8M	Afebrile SE in child with Met Enceph & EP	WCC 0; RCC 810; P 0.25, G 4.2, GR 0.68	HSV PCR neg	MRI – Bilateral high signal densities in globus pallidus. Abnormalities seen previously	Met Enceph & EP
47) 2M	Afebrile seizures	WCC 2; RCC 294; P 0.5, G 2.6, GR 0.71	HSV PCR ND	CT & MRI- N	New onset EP
48) 9Y	Afebrile SE In child with Met Enceph & EP	LP ND	LP ND	MRI - no acute changes	Afebrile SE in child with Met Enceph & EP
49) 3Y	Afebrile focal seizures	Smear ++++ pus cells (surgical specimen); P NR, G NR; CSF culture Pneumo pos	HSV PCR ND	CT - Right temporal lobe abscess	Pneumococcal abscess
50) 5Y	Acute cerebellitis	WCC 0; RCC 0; P 0.28, G 3.1, GR ND	HSV PCR neg	CT - N	Acute cerebellitis
51) 14Y	Drug overdose	LP ND	LP ND	CT - N	Deliberate drug overdose

N = Normal, NR=not recorded, ND= not done

CSF=cerebrospinal fluid, LP= lumbar puncture, WCC=white cell count, RCC=red cell count, N=neutrophils, L=lymphocytes, M=monocytes, DC=degenerated cells, P=protein, G=glucose, GR=glucose ratio, PCR=polymerase chain reaction, BC= blood culture, HSV= herpes simplex virus, CMV= cytomegalovirus, pos=positive, neg=negative, TB= tuberculous, Pneumo=Pneumococcal, Meningo = Meningococcal, Entero= Enterovirus

CT=computed tomography, MRI=magnetic resonance image

BM=bacterial meningitis, VE=viral encephalitis, LRTI=lower respiratory tract infection, EP= epilepsy, CP= cerebral palsy, SE=status epilepticus, VP=ventriculoperitoneal, FC=febrile convulsion, ADEM=acute disseminated encephalomyelitis, Met Enceph=Metabolic encephalopathy