**Supplementary Table e-1:** Clinical features of young children with autoimmune relapsing symptoms post-herpes simplex encephalitis

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|  | **HSE** | | | | **AUTOIMMUNE RELAPSE** | | | | |
| **Case,**  **sex, age** | **Symptoms** | **CSF** | **Brain MRI** | **Treatment and response** | **Symptoms** | **Control MRI** | **CSF and immunological studies** | **Treatment** | **Response to immunotherapy, residual deficits at last follow up** |
| **9# M,**  **11 mo** | Fever, status epilepticus | **Day 1:** HSV pos,  WBC 26, prot. ≤45, neg NSAb | **Day 3:** Bilateral PO necrotic lesions with ADC restr, no contrast enhanc | IV ACYC (21 d) complete recovery | **Day 19:** Alternating periods of lethargy and irritability, loss of contact with environment, refractory seizures, status epilepticus. 60 days after onset of HSE: generalized choreoathetosis | **Day 22:** No new necrotic lesions,  encephalomalacia  Expansion of WM abnormalities  Contrast enhanc +++  **Day 110:** encephalomalacia, no enhanc | **Day 19:** HSV neg,  WBC 54, prot. 64,  pos NMDAR Ab (neg serum)  **Day 85:** pos NMDAR Ab (also in serum) | **Day 20:** ACYC,  IV MP, IVIg, RTX, CYC, ketogenic diet  **Day 70:** PEX | Partial improvement of choreoathetosis and level of consciousness after PEX. Seizures controlled with ketogenic diet.  **FU: 9 mo**, developmental delay with decrease of communicative skills and refractory epilepsy |
| **10# M,**  **15 mo** | Fever, status epilepticus | **Day 1:** HSV pos,  WBC 7, prot. ≤45.  **Day 4:** HSV pos,  WBC 55 prot. ≤45 | **Day 5:** Right PO necrotic lesions with ADC restr, meningeal constrast enhanc + | IV ACYC (21 d) complete recovery | **Day 27:** Confusion, irritability, refractory seizures and status epilepticus. 15 days after onset of relapse: generalized choreoathetosis | **Day 27:** Brain CT, progression to encephalomalacia of previous lesions  Contrast enhanc: n/a | **Day 27:** HSV neg, WBC 47, prot. 115, GABAAR Ab  **Day 44:** HSV neg,  pos NMDAR and GABAAR Ab (both also in serum) | **Day 27:** ACYC, IV MP, induced coma  **Day 44:** PEX, RTX | Improvement of level of consciousness and seizures after PEX and RTX.  **FU: 4 mo**, seizure free, minor choreoathetosis Rapidly improving motor and social skills |
| **11# F,**  **20 mo** | Fever, upper respiratory infection, complex seizures | **Day 18:** HSV pos, WBC 12, prot. 76 | Brain CT: right temporal hypointensity. MRI not obtained | IV ACYC (21 d), residual left hemiparesis | **Day 40:** Irritability and hemiballistic movements  **Day 47:** Prominent lingual dyskinesia, encephalopathy and refractory seizures | **Day 72:** No new necrotic lesions,  encephalomalacia  Contrast enhanc: n/a | **Day 52:** HSV neg,  pos NMDAR Ab  **Day 140 and 360:**  pos NMDAR Ab (also in serum) | **Day 52:** ACYC, PEX | Transient improvement after PEX |
| **12# M,**  **6 mo** | Fever, irritability, decreased level consciousness, complex seizures | Spinal tap not performed (coagulopathy)  Diagnosed by blood serology (1st sample: IgM-, IgG low+; 2nd IgM+, IgG++) | **D9**: left temporal and PO necrotic lesions without contrast enhanc | IV ACYC  (13 d) complete recovery | **Day 27:** Decreased level of consciousness, irritability, hypotonia, general choreoathetosis, orolingual dyskinesias | **Day 40**: No new necrotic lesions lesions, No contrast enhanc | **Day 31:** HSV neg,  WBC 29, prot. ≤45  pos NMDAR Ab  **Day 120:** pos NMDAR Ab (also in serum) | **Day 31:** ACYC, IV MP, IVIg  **Day 120**: starting RTX | Almost full recovery of abnormal movements  **FU: 4 mo**, developmental delay |
| **13# F,**  **8 mo** | Fever, decreased level of consciousness, complex seizures | **Day 3:** HSV pos,  WBC 10, prot. 69 | **Day 4**: Bilateral frontal and PO necrotic lesions with ADC restr and contrast enhanc. | IV ACYC  (21 days), started to improve | **Day 17:** choreoathetosis, decreased level of consciousness | **Day 30:** No new lesions; enlargement of previous necrotic lesions  Contrast enhanc: n/a | **Day 24:** HSV neg,  WBC 8, prot. 56  **Day 72:** posNMDAR Ab (also in serum) | **Day 24** ACYC, IVIg repeated courses of IVIg at 72 , 100 and 130 days | Substantial improvement of choreoathetosis after IVIg  **FU: 5 mo**, developmental delay; requires 3 antiepileptics |
| **14# M,**  **15 mo** | Fever, decreased level of consciousness, complex seizures | **Day 1:** HSV pos,  WBC 20, prot. ≤45 | **Day 4**: Left FT necrotic lesions with ADC restr No contrast enhanc. | IV ACYC  (21 days), clear improvement | **Day 34:** insomnia, low grade fever and irritability, 2 days later choreoathetosis, continuous dyskinesias and decreased level of consciousness | **Day 40:** No new necrotic lesions,  Encephalomalacia  Expansion of WM abnormalities.  No contrast enhanc | **Day 38:** HSV neg,  WBC 25, prot. ≤45  NMDAR Ab (also in serum) | **Day 38:** ACYC, IV MP, IVIg, RTX | **FU: day 40,** Just starting immunotherapy |

Table e-1 Legend: Abbreviations: ACYC: Acyclovir, ADC rest: apparent diffusion coefficient restriction, CSF: cerebrospinal fluid, CT: cranial tomography, CYC: cyclophosphamide, d: days, enhanc: enhancement, F: female, FT: frontotemporal, M: male, HSV: herpes simplex virus, IV: intravenous, Ig: immunoglobulin, mo: months, MP: methylprednisolone, neg: negative, NMDAR Ab: N-methyl-D-aspartate receptor antibodies, NSAb: neuronal surface antibodies, n/a: no available, OCB: oligoclonal bands, PEX: plasma exchange, pos: positive, PO: parietooccipital lobes, prot.: CSF total protein in mg/dL, RTX: rituximab, WBC: white blood cell count /µl in CSF, WM: white mater, y: years