Tick-borne encephalitis presenting as major depressive episode: a case report

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Background: European tick-borne encephalitis (TBE) commonly presents with neurological disturbances, whereas primary psychiatric manifestations are rare.

Aim: To report a case of acute TBE presenting as major depressive episode.

Case report: A 72-year-old man had been suffering from fatigue, poor appetite and tremor of the left hand for 2 weeks. Progression of these symptoms made him believe that he had acquired an incurable and fatal disorder. He repeatedly noted in his diary that ‘the end is not far off’. Generalized weakness and fluctuating level of consciousness lead to examination at the Neurologic Department. His psychiatric medical history was unremarkable. Brain MRI, EEG and laboratory examination was normal. Diminished drive, dysthymia, hopelessness and suicidal ideation were found on mental state exam. Diagnosed with major depression he was hospitalized in the psychiatric ward. One day later, he developed a generalized seizure and laboratory findings supported the diagnosis of European TBE (CSF: 13 cells/μL; protein 60 mg/dL; positive TBE-IgM in serum and CSF). Depressive symptoms declined gradually with a combination of psychotherapy, mirtazapin and sertralin. The tremor responded well to propanolol and was seen as unrelated to TBE. He was discharged home 30 days from admission with minimal residual fatigue and low dose mirtazapin.

Conclusion: Acute life-threatening psychiatric manifestations can be the predominant presenting but successfully treatable feature of TBE. We conclude that awareness for this condition should be raised in endemic regions and high-level of suspicion for encephalitis maintained with the occurrence of seizures or focal-neurological deficits in acute psychiatric conditions.

doi:10.1016/j.jns.2015.08.093

Investigation of coagulation behavior using Rotational Thromboelastometry (Rotem®) in patients with neuroinfectious diseases

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Background: Neuroinfectious diseases are recognized to cause severe dysregulation on inflammation and coagulation behaviors. Dengue, one of the major infectious diseases, manifests neurological complications such as encephalitis and encephalopathy. The mosquito-borne viral infection is said to disrupt the coagulation cascade. Rotational thromboelastometry measures the interactions of coagulation factors, inhibitors and cellular components during the phases of clotting and subsequent lysis over time. Detailed analysis of coagulation parameters was investigated using thromboelastometry and standard coagulation parameter in patients with neuroinfectious diseases, such as dengue, from two different countries, i.e. Brunei Darussalam and Germany.

Aim: The information provided by the participants will help to investigate the functional coagulation behaviour in the long term by means of the detailed analysis of coagulation parameters using thromboelastometry during the acute stage of disease.

Methods: Blood samples were collected from patients with neuroinfectious diseases, particularly but not limited to dengue, to investigate the coagulation profile. Serum samples were carefully collected from participants in different countries and were centrifuged at 3000 r.p.m. for 10 minutes. Detailed analysis of haemostatic parameters were subsequently undertaken using ROTEM® analysis.

Results: Interim analysis and preliminary analysis indicate that lab techniques under investigation such as ROTEM® analysis reveal high abnormalities in thromboelastometry and other standard tests.

Conclusion: Neuroinfections are highly important – infectious of the brain and meninges may cause severe disability in patients of any age. Increasingly, comparable to stroke, in neuroinfectious disease the gold standard for survival is rapid diagnosis as basis for rapid treatment. Therefore: Time is brain.

doi:10.1016/j.jns.2015.08.094
Do adjunctive corticosteroid and aspirin improve the outcome of tuberculous meningitis?

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Background: Corticosteroid and aspirin have been reported to improve the outcome of tuberculous meningitis (TBM) but their relative efficacy of corticosteroid, aspirin and combination of both have not been evaluated.

Objective: To compare the outcome of patients with TBM receiving adjunctive aspirin, aspirin + corticosteroids or none of these therapies.

Patients and methods: In a retrospective hospital based study, consecutive patients with TBM during 2008-2014 were included after ethical clearance. The diagnosis of TBM was based on clinical, cerebrospinal fluid (CSF), MRI, AFB and PCR findings. The severity of meningitis was graded into stage I, II and III. They received 4 drugs (HRZE) antitubercular treatment with 150 mg/day aspirin (Group I) or prednisolone (0.5mg/kg/d) for 1mo plus aspirin (Group II) or none of these adjunctive therapies (Group III). Outcome was defined at 3 months into death, poor or good.

Results: 135 patients with TBM were included whose median age was 36.4 years and 49.6% were females. 29.6% patients had stage I meningitis, 54.8% stage II and 15.3% stage III meningitis. Group II patients had more severe illness compared to group I and III (P<0.002).

At 3 months, 24% patients died; 18.2% in group I, 18% in group II and 34.1% in group III. Complete recovery was more frequent in group II (48.8%) compared to group I (30.6%) and group III (25.9%). Death and functional outcome however were not significantly different in between the groups.

Conclusion: Adjunctive steroid plus aspirin therapy in TBM seems to offer survival and outcome benefit.

doi:10.1016/j.jns.2015.08.095

Deficit sciatica post varicella zoster virus infection

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Objective: Remembering through a case report the neurologic involvements of VZV infection implicated indirect mechanism.

Case report: A 64-year-old was admitted for bilateral sciatica L5 and S1 with bladder disorders progressively installed two months after intercostal zoster. The examination showed flaccid areflexic paraparesis with a sensory level D10-D11. The spinal MRI showed medullar hypersignal D11-D12 on T2 weightig with meningeal and roots contrast enhancing. CSF study was consistent with aseptic lymphocytic meningitis with negative VZV PCR. The EMG showed lower limb polyradicular lesions. The diagnosis of post herpetic meningomyeloradiculitis was made. Patient improved under aciclovir and corticosteroid. He consulted six months later for recurrence of the same symptoms concomitant to radiculalgia. The resumption of corticosteroids was marked by clinical and radiological improvement.

Discussion: Neurological complications of varicella zoster virus (VZV) are rare and they are dominated by encephalitis. Direct mechanism is implicated. Myeloradiculitis involving indirect mechanism is rarely reported. Sciatica with neurological deficit can be the first manifestation.

Conclusion: Remembering through a case report the neurologic involvements of VZV infection implicated indirect mechanism.

doi:10.1016/j.jns.2015.08.097
Refractory CNS infections often require intrathecal antibiotics but the safety of this practice has not been determined. We hereby describe our experience with intrathecal antibiotics in a series of patients admitted to a neurologic intensive care unit at a university center.

**Methods:** Retrospective case series of all patients with refractory CNS infections admitted to a neurosciences ICU at a university hospital over 7 years. The following data were abstracted from the medical records: demographics, diagnosis, type of infection, organism, antibiotic used, time to negative cultures, and complications associated with intrathecal antibiotics.

**Results:** A total of 26 patients were treated 12 (44%) male. Median age was 54 years old. The most common diagnosis was subarachnoid hemorrhage in 10/26 (38%), followed by brain tumors 6/26 (23%), intracranial hemorrhage 3/26 (12%), shunt infection 3/26 (12%), traumatic brain injury 2/26 (7%), primary meningitis and cerebral cyst 1/26 (4%) each. The most common organisms were gram negatives in 14/26 (54%), gram positives in 6/26 (23%), and coagulase negative staphylococcus in 6/26 (23%). The median time to CSF culture sterility was 8 days (range 1-14). The antibiotics used were vancomycin in 10/26 (38%), gentamicin in 15/26 (58%), and amikacin in 1/26 (4%). No immediate complications occurred.

**Conclusions:** Intra-thecal administration of antibiotics in patients with refractory CNS infections appears to be safe and appears to be effective at achieving CSF sterility.

doi:10.1016/j.jns.2015.08.098

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**Fatal PML in a patient treated with compounded dimethyl fumarate with only modest lymphocytopenia**

**Background:** Since the 1950s fumaric acid esters (FAEs) have been approved as treatment for multiple sclerosis. FAEs have immunomodulatory and immunosuppressive effects and although they lead to a reduction of peripheral blood lymphocyte counts, opportunistic infections appear to be very rare. However, since 2013 several cases of progressive multifocal leukoencephalopathy (PML) were reported in patients with sustained and severe lymphocytopenia. Recently, two PML cases without severe lymphocytopenia were also reported.

**Objective:** Present the case of a psoriasis patient with PML after two years treatment with Psorinovo (DMF compounding pharmacy, Mierlo-Hout, the Netherlands). (Nieuwkamp et al, NJEM 2015; 372:1474-1476)

**Patients and methods:** In June 2012 a 64 year old Dutch woman with psoriasis started treatment with Psorinovo 240 mg t.i.d. Since July 2013 the dose was reduced to 240 mg b.i.d. She received no other systemic immunosuppressive treatment and was seronegative for HIV. During the treatment period, her total leukocyte counts remained within normal range.

**Results:** In July 2014 the patient developed progressive apraxia. Due to atypical CT and MRI imaging findings, no history of leukocytopenia and negative JC virus PCR in CSF, PML was rejected and the diagnosis of atypical ischemic stroke was made and Psorinovo was stopped. Her condition continued to deteriorate and MRI images were suggestive of PML-IRIS. Posthumously the diagnosis PML was established by PCR and immunohistochemistry.

**Conclusion:** Physicians should be alert for PML in patients treated with FAEs, both in lymphocytopenic and non-lymphocytopenic patients.

doi:10.1016/j.jns.2015.08.099

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**Guillain-Barré syndrome in the course of dengue**

**Background:** Guillain-Barré syndrome in the course of dengue fever and macular rash. He was diagnosed as having dengue, based on clinical manifestations and specific IgM titres.

Ten days after the first symptoms of dengue, the patient developed muscle weakness, followed by tetraplegia and respiratory failure. Electromyography with electrical data demyelinating neuropathy and the cerebrospinal fluid associated with albuminocytologic dissociation. These neurologic findings were consistent with a diagnosis of Guillain-Barré–polyneuropathy acute inflammatory syndrome, the patient was treated with immunoglobulin and methylprednisolone. Mechanical ventilation was initiated after admission and maintained for 21 days. After 30 days of hospitalization he left the hospital with muscle weakness and loss of patellar and ankle reflexes.

doi:10.1016/j.jns.2015.08.100