CNS INFECTIONS

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MENINGITIS, ENCEPHALITIS, MYELITIS AND ADEM IN CHILDREN: AUTOMATED CASE ASCERTAINMENT (CHAT ANALYSIS) IN REAL-TIME

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Introduction: Pediatric CNS infections may present with a variety of signs and symptoms, which may be subtle or inconsistent. Clinical diagnoses may vary depending on the assessor. For syndromic surveillance and reliable public health data, standardized case definitions should be implemented at the point-of-care (POC).

Methods: An automated case ascertainment tool (ChAT) was programmed based on published case definitions for aseptic meningitis (ASM), encephalitis (ENC), myelitis (MYE), and acute disseminated encephalomyelitis (ADEM). From 2010-2013, a total of 521 consecutive cases of suspected CNS infection (51.2% male, median age: 6.4 years, range 0.03; 17.9 years) were assessed prospectively. An independent quality management team performed structured neurologic assessments using ChAT in real-time. Case classifications based on ChAT analysis were compared to: chart review applying the same standardized case definitions retroactively, versus screening of ICD-10-coded discharge diagnoses.

Results: With ChAT analysis, 188 cases fulfilled at least one case definition, compared to 170 cases by retrospective chart review. Review of ICD-10-coded discharge diagnoses revealed 83 cases. Positive and negative percent agreement between ChAT and retrospective analysis were 58.7% (95%CI =52.8-64.4%) and 97.9% (95%CI =97.1-98.5%; p<0.0001). Cohen's kappa coefficients comparing ChAT to retrospective analysis were 0.86 (ASM), 0.62 (ENC), 0.0 (MYE) and 0.69 (ADEM), respectively.

Conclusions: Retrospective chart review and ICD-10-based screenings may be missing cases due to insufficient data. Taking case definitions to the POC will provide more information for immediate and well-standardized case classifications eliminating observer bias and inter-rater variability.

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HERPES-SIMPLEX ENCEPHALITIS IN PATIENTS WITH ONCO-HEMATOLOGICAL DISEASE

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Herpes-simplex encephalitis (HSE) is a well-known but rare complication in patients after bone marrow transplantation (BMT) or with CNS tumours. The aim of this study was to describe three patients with HSE during the course of an onco-hematological disease (OHD).

Material and methods: From a sample of 18 confirmed PCR-positive cases of HSE in CSF seen over a period of 12 years, three patients with OHD were identified.

Results: Underlying disease and treatment: brainstem tumour and radiation/steroid therapy (1), maxillary embryonal rhabdomyosarcoma with parameningeal invasion and chemotherapy (1), and ALL and post-BMT immunosuppression (1). The presenting symptom was altered consciousness in all and two patients had focal motor seizures. CSF showed pleocytosis with raised proteins in two. CFS was PCR-positive for HSV-II in two and HHV6 in one. Brain MRI showed hyper intense signal on T2 and FLAIR in the corticosubcortical regions while the frontal and temporoinsular regions were unenhanced. The image was bilateral in two and asymmetrical in one. Only one had a bleeding complication. The EEG showed periodic, lateralized, epileptiform discharges in two cases. The patients were put on IV acyclovir for 21 days. All patients showed severe motor and neurocognitive involvement after treatment that had not been present before HSE onset.

Conclusion: As in all acute encephalopathies, early diagnosis and treatment of HSE is crucial. Immunosuppression may play a role in the reactivation of HSV. Another mechanism may be the viral reactivation induced by radiotherapy, when this includes the Gasser ganglion, as in the brainstem tumour patient.

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EXOGENOUS BDNF IMPROVES ENDOGENOUS NEUROGENESIS FOLLOWING EXPERIMENTAL STREPTOCOCCUS PNEUMONIAE MENINGITIS

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Despite of the usage of effective antibiotics, the occurrence of mortality and neurological sequelae following streptococcus pneumonia meningitis remains high. We investigated neurogenesis effect of brain-derived neurotrophic factor (BDNF) on hippocampus dentate gyrus (DG) and subventricular zone (SVZ) in streptococcus pneumonia meningitis via double-labeling immunofluorescene with BrdU, DCX and NeuN. Our results showed that the area of DCX positive cells decreased in DG of infected rats treated with saline compared with normal control rats($p<0.05$). However, the area of DCX positive cells from infected rats treated with BDNF got close to normal control level($p>0.05$). After adjuvant therapy with exogenous BDNF, the population of BrdU positive cells increased in infection and normal control rats both in DG($p<0.01$) and SVZ($p<0.05$) especially in infection rats($p<0.05$) compared to that of corresponding control rats, respectively. We found BrdU/DCX positive cells in infected rats treated with BDNF and migrated into deep layer of DG, and BrdU/DCX positive cells increased compared with normal control rats treated with BDNF, normal control and infected rats treated with saline($p<0.01$). And BrdU/NeuN-labeled neurons in DG were also found in infected rats treated with BDNF($p<0.05$), while none in infected rats treated with saline. These findings support the hypothesis that the proliferation of endogenous NSCs was activated by streptococcus pneumonia meningitis, but it impaired the differentiation of endogenous NSCs that the administration of exogenous BDNF might improve neurogenesis of endogenous NSCs in experimental streptococcus pneumonia meningitis, a finding that may be a promising therapy in recovering neurological deficits and decreasing mortality during brain injury.

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CLINICORADIOLOGICAL OUTCOMES IN CHILDREN WITH SOLITARY NEUROCYSTICERCOSIS WITH AND WITHOUT ALBENDAZOLE THERAPY: A RETROSPECTIVE CASE RECORD ANALYSIS.

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Introduction: Neurocysticercosis is a common cause of seizures in developing countries. This study analyses the seizure and radiological outcomes in children with solitary neurocysticercosis from a north Indian tertiary care hospital.

Materials and Methods: The case records of children at a tertiary care hospital in New Delhi from January 2003 to December 2006 (Group A, 171; did not receive albendazole) and from January 2008 to June2013 (Group B, 512; received albendazole) were reviewed. Children aged 1 to 12 years, newly diagnosed as probable or definite solitary neurocysticercosis on contrast-enhanced CT head, presenting with seizures with at least 6 months follow-up and an available follow-up CT head, were included. Those with calcified lesions on initial CT head were excluded.

Results: Group B had significantly more resolution (complete disappearance on follow up CT) of lesions (67.3% versus 30.4%, p<0.0001) as compared to group A. However there was no significant difference in calcification observed in group A and B (30.4 and 25.9% respectively. P=0.25). Overall patients with calcification or complete disappearance were significantly more in-group B compared to A (93.3% versus 60.8%, p<0.0001). Breakthrough seizures were significantly more in the group A (23.9% versus 7.2%, p<0.0001).Overall in 2 groups, lesions

that got calcified had significantly more breakthrough seizures than non-calcified ones (21.6% versus 7.6%, p<0.0001).

Conclusions: Albendazole therapy results in improved seizure control and expedites radiological resolution in children with neurocysticercosis. Children with calcified lesions are at high risk for seizure recurrence and may warrant longer anti-epileptic therapy.[1]

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CSF CULTURES / DRUG SENSITIVITY IN PEDIATRIC TBM - EXPERIENCE FROM A TERTIARY-CARE HOSPITAL IN INDIA

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Introduction: Tuberculous meningitis (TBM) in children is difficult to diagnose / confirm as the yield of CSF culture is low and is delayed for weeks. India is estimated to have 20% of all multi-drug resistant (MDR) TB worldwide. This tertiary hospital-based study was carried out to ascertain the usefulness of CSF culture in suspected TBM and look for drug resistance.

Methods: Pediatric TBM patients admitted to the hospital were identified from the hospital's medical records and Microbiology Department records. Chart reviews helped to classify patients into probable, possible and not TBM based on recent TBM consensus criteria (1). The BACTEC MGIT 960 system was used for culture. Drug sensitivity testing (DST) was done if requested by the referring clinician.

Results: Over a 3 years period CSF from 48 patients was sent for TB culture. 32 were classified probable, 9 as possible and 7 as not TBM. 20/41 (49%) suspected TBM patients had positive cultures – 16/32 (50%) probable cases and 4/9 (44%) possible cases.

DSTs were performed in 15/20 positive CSF cultures. In 7/15 (47%) the TB bacilli were sensitive while in 8 (53%) they were resistant- MDR in 7 and extensively drug resistant (XDR) in 1. Only 1/5 drug-naïve newly diagnosed TBM was MDR vis-à-vis 7/10 of those already on treatment.

Conclusion: Positive cultures are seen in half of childhood TBM patients in line with other Indian reports (2). More than half were MDR/XDR probably due to a referral bias. Expectedly drug-naïve cases were more likely to be drug sensitive.

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CLINICAL PRESENTATION AND PROGNOSIS OF PEDIATRIC ENCEPHALITIS: EXPERIENCE OF A KOREAN SINGLE TERTIARY CENTER

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Purpose: This study was performed to investigate the clinical presentations, diagnostic findings and prognosis of paediatric patients with the broad definition of "encephalitis", that is inflammation of brain, in a single Korean tertiary center.

Methods: We retrospectively analysed medical records of patients who had been diagnosed with encephalitis from January 2000 to July 2013 at the Asan Medical Center Children's Hospital. We classified encephalitis in three categories of etiology which are infectious, para-infectious and primary inflammatory. The initial presentation, radiological and electroencephalographic findings, treatments and outcomes were reviewed.

Results: During the 13-year study period, we found 200 paediatric cases of encephalitis. 131 (65.5%), 48 (24.0%), and 21 (10.5%) cases were classified as infectious, para-infectious and primary inflammatory encephalitis, respectively. Most of cases presented with fever (n=125), altered mentality (n=101), seizures (n=105) and motor dysfunction (n=39). With diagnostic evaluations including CSF study, MRI and EEG, 183 cases (91.5%) had specific diagnosis and got definitive treatment. Specific pathogens were proved in only 32 (24.4%) patients from 131 infectious encephalitis. 126 (63.0%) cases recovered without sequela, 51 (25.5%) cases with sequelae and 8 (4.0%) cases were expired. Expired cases included 6 with infectious encephalitis, 1 with ADEM and the other with Reye syndrome.

Conclusion: Most of paediatric encephalitis patient came with altered mentality and febrile illness and infectious encephalitis gets a great part among them. But many cases need additional effort to find specific aetiologies of encephalitis. Considering the high mortality and morbidity of the paediatric encephalitis, prompt evaluations and appropriate treatment should be implemented.

FP69

IS THAT DIAGNOSTIC LUMBAR PUNCTURE NECESSARY?

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Introduction: We hope to stimulate discussion about the role of diagnostic lumbar puncture (LP) in suspected bacterial meningitis. Raised intracranial pressure (RICP) almost always accompanies bacterial meningitis and brain herniation can be precipitated by LP.

Methods: A 10-year-old girl presented with severe progressive headache, photophobia, vomiting, neck stiffness but no fever, rash. Past medical history included pneumococcal septicaemia with meningitis, at ages 5 & 8 years respectively with full recovery. Immunodeficiency screen was negative.

During this admission, there were no signs of RICP. LP revealed purulent CSF with gram-positive cocci (Pneumococcus serotype F7). One hour post LP she collapsed with generalised extensor posturing and cyanosis, requiring ventilation. CT head post-LP was reported normal. She subsequently developed asymmetric pupils. MRI brain showed tonsillar herniation with patchy infarction of lower brain stem, cerebellum, upper cervical cord with early hydrocephalus. Emergency foramen magnum decompression with ventricular drainage was performed. She regained consciousness but was paralysed below mid-pontine level with bilateral facial/bulbar palsies, respiratory failure, flaccid quadriplegia and absent sensory/autonomic function. One year on she is ventilator dependent with no significant improvement in function.

Discussion: We highlight the need for caution before diagnostic LP in bacterial meningitis. Rapidly worsening headaches and vomiting may reflect RICP even without clinical signs. Normal CT brain does not exclude RICP. In suspected bacterial meningitis, empirical treatment should be started after blood cultures until neurological status is confidently ascertained. CSF microbiological analyses are good proxies at a later, safer time.

FP70

PREDICTORS OF NEUROPSYCHIATRIC MANIFESTATIONS AMONG CHILDREN WITH DENGUE INFECTION

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Introduction: Early recognition and improvement in the understanding of the wide spectrum of manifestations in dengue will provide prompt and appropriate management of cases. This study aimed to determine factors predictive of the development of neuropsychiatric manifestations among children with dengue infection

Methods: All children with laboratory-confirmed (positive NS1 antigen or serum IgM for dengue) dengue admitted at the Paediatrics wards of a tertiary government hospital were enrolled. Age, dengue type and severity, presence of malnutrition, fever severity were analysed to determine association with the development of neuropsychiatric manifestations such as encephalitis, encephalopathy, psychosis, acute disseminated encephalomyelitis (ADEM) and Guillain-Barre syndrome (GBS).

Results: Eight (13.6%) children, (mean age of 10.5 years, 6 males) with dengue developed neuropsychiatric manifestations, namely: encephalitis (n=3), encephalopathy (n=2), ADEM (n=1), GBS (n=1) and psychosis (n=1). Age, dengue severity and type, malnutrition, and fever severity were not significantly related with these manifestations. Seven had secondary type of dengue. Five were classified as dengue fever and three as dengue haemorrhagic fever III. Seven were malnourished. Mean WBC count, hematocrit and platelet count were 11±5, 0.37±0.07 and 252±153, respectively. One patient died (12.5%) due to increased intracranial pressure.

Conclusion: In an endemic region, dengue infection should be a foremost differential diagnosis of encephalitis, GBS, ADEM, psychosis and encephalopathy, despite absence of thrombocytopenia and leukopenia. This study did not show significant predictive factors in the development of these neuropsychiatric manifestations.

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NEUROLOGICAL MANIFESTATIONS IN CHILDHOOD BAGGIO-YOSHINARI SYNDROME (LYME DISEASE-LIKE SYNDROME IN BRAZIL)

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Abstract: In the present study, we report three occurrence of Baggio-Yoshinari Syndrome in children from the Brazilian Southeast Region. Lyme disease-like syndrome or Brazilian Baggio-Yoshinari is an exotic and emerging zoonosis not transmitted by ticks belonging to the Ixodesricinus, complex, caused by spirochetes with atypical and latent morphology, which originates clinical manifestations similar to those, observed in Lyme disease, except for the occurrence of clinical relapses and autoimmune disorders.

Method: Were described three cases of Baggio-Yohinari Syndrome, two boys (2 and 8 years) and a girl (12 years).

Discussion: No child had erythema migrans, but had a history of having been bitten by ticks, two from pets and one from the countryside. The three children had neurological manifestations, two with polyradiculoneuritis and one with subacute lymphocytic meningitis, none of them had erythema migrans. Borreliosis was investigated by immunohistochemistry by the group of rheumatology. All children were treated with Ceftriaxone for 14 days and then with Dicloxacillin, except the youngest child who was treated with Amoxicillin, for four weeks. The girl developed Jarisch-Herxheimer reaction on the third day of treatment.

Conclusion: The child neurologist should always investigate history of contact with ticks even in the absence of erythema. In Brazil, cases with clinical manifestations resembling Lyme disease usually have positive serological tests, a good response to antibiotics, and serological cure

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OPPORTUNITIES OF EMERGENCY CHEMOPROPHYLAXIS OF TICK-BORNE ENCEPHALITIS IN CHILDREN

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Emergency specific prevention of tick-borne encephalitis (TBE) using intramuscular administration of anti-tick immunoglobulin should be performed directly after tick bite in persons non-immunized against TBE as well as in those seeking medical advice within 96 hours after bite. However, low efficacy of specific TBE prevention, high risk of parenteral contamination after blood preparation administration triggered development of a new approach to such TBE prevention. The aim of the study was an assessment of efficacy of antiviral drug Anaferon for children (AnC) for emergency chemoprophylaxis of TBE in children. The study enrolled 980 subjects aged 2-17 years seeking medical advice after tick bite. AnC is an endogenous interferon inductor (IFN-alpha and IFN-gamma) containing affinity purified antibodies to human IFN-gamma in release active form. It has been approved for use starting from the age of 1 month. All children enrolled into the study were analyzed for blood TBE virus and level of blood specific immunoglobulins M and G using, blood interferon level (IFN-alpha, -beta and -gamma). Analysis of immunoglobulins and IFN was performed twice: prior to emergency prophylaxis and one month later. It was shown that emergency chemoprophylaxis of TBE in children using Anaferon for children is effective and safe in patients of different age and cause of the disease.

FP73

PARADOXICAL REACTION IN THE CENTRAL NERVOUS SYSTEM AFTER TUBERCULOSIS TREATMENT IN AN IMMUNOCOMPETENT CHILD.

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Introduction: A paradoxical reaction (PR) after an appropriate initial response to tuberculostatic treatment should be considered in patients with worsened clinical and neuroimaging features. Our purpose was to present a case of a PR in the central nervous system (CNS) in an immunocompetent child.

Case description: A previously healthy 15-year-old girl was admitted for a 30-day history of right-hand tremor. MRI showed a gadolinium-enhancing mesencephalic lesion. Initial blood analyses were normal. Human immunodeficiency virus (HIV) infection and primary immunodeficiency diseases were ruled out. Chest radiography showed interstitial infiltrates. Bacilloscopy was positive. Miliary tuberculosis with CNS involvement was diagnosed and tuberculostatic (four drugs) and corticosteroid treatment was started. At 8 weeks after treatment initiation, the patient worsened. Vision loss in the left eye (5/10) with normal fundoscopy, left III-cranial-nerve palsy, and right hemiparesis were observed. MRI showed supratentorial lesions and brainstem edema. Brain biopsy only revealed reactive gliosis. The girl was put on high-dose corticosteroids with a good clinical response and improved neuroimaging.

Discussion: Data on PR reactions in neurotuberculosis in immunocompetent hosts are scarce, especially in children. A PR after tuberculostatic treatment is well known in HIV patients. The incidence in immunocompetent children is 10-14%. The most commonly reported extrapulmonar involvement is in the lymph node. Despite data on the poor prognosis of neurotuberculosis, outcome was excellent in our patient. Awareness of this entity is important, as modified management may be necessary in some cases.

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ETIO-PATHOGENETIC THERAPY OF VIRAL ENCEPHALITIS IN CHILDREN

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Introduction: There are very few antiviral medicines which are allowed for use in children.

Aim: To evaluate the efficiency of Viferon in complex therapy of children with viral encephalitis (VE). **Methods:** 75 patients with VE from 3 months to 3 years of old. The main group - 57 people, got a complex antiviral therapy of wide spectrum – recombinant interferon-a2 Viferon, which is allowed for use in children from birth. Viferon provides antiviral and immune modulatory effect and it suppresses viral replication. Children with proven diagnosis got suppositories Viferon. The comparison group contained 18 patients with VE, comparable on sex, age groups, cause of the disease and etiology, who got complex therapy (acyclovir, cytoflavin, methylprednisolone). Monitoring of neurological status, virology, radiology, immunology were performed.

Results: Etiology of VE**:** 68% all herpes viruses, 10, 7% enteroviruses, 2, 6% virus of tick-born encephalitis and rubella virus. Acute cause VE was in 74, 7% cases, lingering cause – in 12%, chronicle - 9, 3%.

Discussion: A significant reduction in the duration of common infectional syndrome, viremia, repeated exacerbations, a reduction in the frequency of residual neurologic deficit and cystic-gliosis-atrophic process in the central nervous system were seen along with a significantly accelerated restoration of normal production interferon-α in blood. Side effects of Viferon were not seen. The use of suppositories Viferon in complex therapy children with VE under 3 old is safe, effective and helps to improve the disease outcomes.