Volume 3, Issue 7

CIDS Newsletter

July 2016

CLINICAL INFECTIOUS DISEASES SOCIETY

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Editor's note

Dear CIDS members

Hope all of you have registered for CIDSCON in Varanasi on Aug 26-28. Please plan on attending the annual general body meeting scheduled for 27th evening.

Sincerely

Ram Gopalakrishnan

Photo quiz

A 26 yrs lady with multi-drug resistant (MDR) tubercular meningitis (TBM) had been started on 2nd line ATT 8 months ago. After initial improvement, she presented with heaviness of the head, slurring of speech and slowness of activities for 15 days. She was currently on para-aminosalicyclic acid, cycloserine, ethionamide and linezolid. There was no history of vomiting, fever or any focal neurological deficit.

Investigations revealed a normal hemogram and thyroid function tests. MRI brain was done (see figure 1 below)

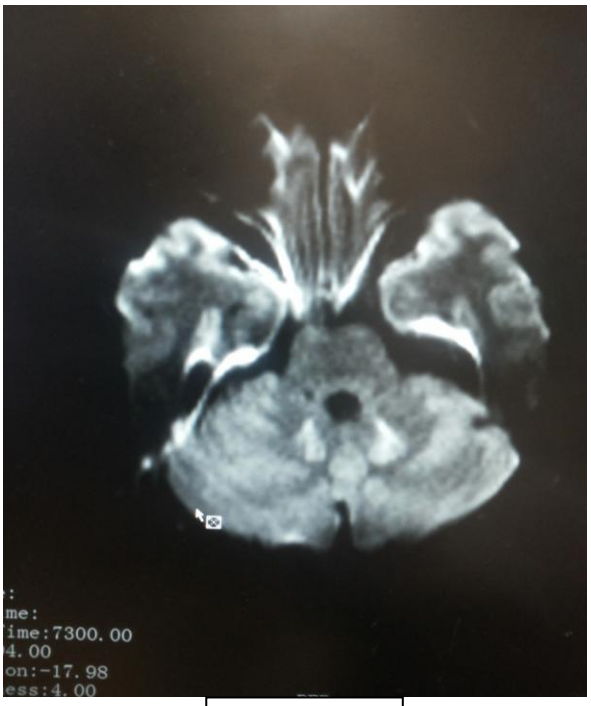

Figure 1

What is your diagnosis?

Snippets from the literature

A Worldwide Map of *Plasmodium falciparum* K13-Propeller Polymorphisms

N Engl J Med 2016;374:2453-2464

Recent gains in reducing the global burden of malaria are threatened by the emergence of *Plasmodium falciparum* resistance to artemisinins. The discovery that mutations in portions of a *P. falciparum* gene encoding kelch (K13)–propeller domains are the major determinant of resistance has provided opportunities for monitoring such resistance on a global scale.The authors analyzed the K13-propeller sequence polymorphism in 14,037 samples collected in 59 countries in which malaria is endemic. In Asia, 36.5% of the K13 mutations were distributed within two areas — one in Cambodia, Vietnam, and Laos and the other in western Thailand, Myanmar, and China — with no overlap. In Africa, they observed a broad array of rare nonsynonymous mutations that were not associated with delayed parasite clearance.

No evidence of artemisinin resistance was found outside Southeast Asia and China, where resistance-associated K13 mutations were confined. So far, Africa - and India- are free of artemsisinin resistance.

Corticosteroids for managing TBM

Cochrane Database Syst Rev. 2016; 4 (CD002244)

Nine trials that included 1337 participants (with 469 deaths) met the inclusion criteria.At follow-up from three to 18 months, steroids reduce deaths by almost one quarter (RR 0.75, 95% CI 0.65 to 0.87; nine trials, 1337 participants, high quality evidence). Disabling neurological deficit is not common in survivors, and steroids may have little or no effect on this outcome (RR 0.92, 95% CI 0.71 to 1.20; eight trials, 1314 participants, low quality evidence). There was no difference between groups in the incidence of adverse events, which included gastrointestinal bleeding, invasive bacterial infections, hyperglycaemia, and liver dysfunction.

One trial followed up participants for five years. The effect on death was no longer apparent at this time-point (RR 0.93, 95% CI 0.78 to 1.12; one trial, 545 participants, moderate quality evidence); and there was no difference in disabling neurological deficit detected (RR 0.91, 95% CI 0.49 to 1.69; one trial, 545 participants, low quality evidence). One trial included human immunodeficiency virus (HIV)-positive people. The stratified analysis by HIV status in this trial showed no heterogeneity, with point estimates for death (RR 0.90, 95% CI 0.67 to 1.20; one trial, 98 participants) and disability (RR 1.23, 95% CI 0.08 to 19.07; one trial, 98 participants) similar to HIV-negative participants in the same trial.

Corticosteroids reduce mortality from tuberculous meningitis, at least in the short term. Corticosteroids may have no effect on the number of people who survive tuberculous meningitis with disabling neurological deficit.

Symptomatic Dengue in Children in 10 Asian and Latin American Countries

N Engl J Med 2016; 374:1155-1166

The control groups in two phase 3 trials of dengue vaccine efficacy included two large regional cohorts that were followed up for dengue infection. The authors monitored acute febrile illness and virologically confirmed dengue (VCD) in 3424 healthy children, 2 to 16 years of age, in Asia. Acute febrile episodes were determined to be VCD by means of a nonstructural protein 1 antigen immunoassay and reverse-transcriptase–polymerase-chain-reaction assays. Approximately 10% of the febrile episodes in each cohort were confirmed to be VCD, with 319 VCD episodes (4.6 episodes per 100 person-years) occurring in the Asian cohort.

The percentage of VCD episodes requiring hospitalization was 19.1% in the Asian cohort. An effective vaccine for dengue is a public health priority, given how common the disease is.

Dengue during pregnancy and adverse fetal outcomes

Lancet 2016 Volume 16, No. 7; p857-865, July 2016

This meta-analysis looked at outcomes after dengue in pregnancy. For miscarriage, the OR was calculated to be 3·51 (95% CI 1·15–10·77, I^2=0·0%, p=0·765) and for stillbirth the crude relative risk to be 6·7 The OR was 1·71 (95% CI 1·06–2·76,I^2=56·1%, p=0·058) for preterm birth and 1·41 (95% CI 0·90–2·21, I^2=0·0%, p=0·543) for low birthweight.

While not associated with congenital abnormalities, dengue clearly increases adverse fetal outcomes.

Tenofovir for Preventing Hepatitis B Transmission from Mother to Infant

N Engl J Med 2016 Jun 16; 374:2324

A total of 200 HBV-infected pregnant women (age range, 20–35) positive for hepatitis B e antigen (HBeAg) and with baseline HBV DNA >200,000 IU/mL were randomized to usual care (control) or tenofovir disoproxil fumarate (TDF; 300 mg daily from 30 to 32 weeks' gestation until postpartum week 4). All infants received immunoprophylaxis shortly after birth. At postpartum week 28, mother-to-child transmission was significantly lower in the TDF group than the control group, 0% versus 7% (*P*=0.01). Maternal and neonatal safety profiles were similar between groups.

Tenofovir in the third trimester is now part of guidelines in patients who fit the above criteria.

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Seven-Year Efficacy of RTS,S/AS01 Malaria Vaccine among Young African Children

N Engl J Med 2016;374:2519-252

The most advanced of the current candidates against *P. falciparum* is RTS,S/AS01, a recombinant vaccine against the pre-erythrocytic stage of the parasite in which regions of *P. falciparum* circumsporozoite protein are fused to hepatitis B surface antigen. The vaccine efficacy for 3 doses, as assessed by negative binomial regression, was 4.4% (95% confidence interval [CI], −17.0 to 21.9; P=0.66) in the intention-to-treat analysis and 7.0% (95% CI, −14.5 to 24.6; P=0.52) in the per-protocol analysis. Vaccine efficacy waned over time (P=0.006 for the interaction between vaccination and time), including negative efficacy during the fifth year among children with higher-than-average exposure to malaria parasites.

The wait for an effective malaria vaccine continues.

Predominance of *Lactobacillus* spp. among patients who do not acquire multidrug-resistant organisms

Clin Infect Dis. (2016)doi: 10.1093/cid/ciw426

Adult patients admitted to 5 general medical-surgical floors at a 649-bed, tertiary care center, were classified according to in-hospital antimicrobial exposure and MDRO colonization status. Hospitalized patients (n =44) had reduced microbial diversity and a greater abundance of *Escherichia* spp. and *Enterococcus* spp. compared to healthy controls (n =26). MDRO-patients had consistently higher *Lactobacillus* spp. abundance compared to the MDRO+ group (LDA score =3.97; *P* =0.04).

Microbiome remediation with therapy with say Lactobacillus to prevent MDRO acquisition may be around the corner.

Daptomycin seems safe and effective in children

(courtesy Dr Ashwini Choudhary)

The Pediatric Infectious Disease Journal May 2016
Vol. 35 - Issue 5: p 511–516

This subgroup analysis of the European Cubicin Outcomes Registry Experience evaluated the safety and effectiveness of daptomycin in children and adolescent patients (<18 years). Forty-nine (60.5%) of 81 patients completed daptomycin therapy without further antibiotics, 27 (33.3%) switched to another antibiotic, 4 (4.9%) discontinued because of adverse events (AEs) and 1 (1.2%) discontinued because of other reason. Overall, 75 (92.6%; 95% confidence interval: 95.2–100.0%) patients achieved clinical success; 39 of 41 (95.1%) patients receiving daptomycin monotherapy and 36 of 40 (90.0%) patients receiving concomitant antibiotics. Six (7.4%) patients reported AEs, including 1 patient with increased blood creatine phosphokinase. Three (3.7%) patients had serious AEs; 1 (1.2%) had a serious AE possibly related to daptomycin.

Guideline watch

IDSA/SHEA guidelines on Implementing an Antibiotic Stewardship Program

Clin Infect Dis. (2016) 62 (10):e51-e77.doi: 10.1093/cid/ciw118

Salient features and recommendations:

- recommend preauthorization and/or prospective audit and feedback as core elements
- suggest against relying solely on didactic educational materials
- develop facility-specific clinical practice guidelines for common and specific syndromes
- reduce the use of antibiotics associated with a high risk of CDI
- suggest the use of strategies (eg, antibiotic time-outs, stop orders) to encourage prescribers to perform routine review
- incorporation of computerized clinical decision support
- suggest against the use of antibiotic cycling

- hospitals implement PK monitoring and adjustment programs for aminoglycosides and vancomycin
- advocate for Alternative Dosing Strategies Based on PK/Pharmacodynamic Principles
- increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics
- reduce antibiotic therapy to the shortest effective duration
- suggest selective and cascade reporting of antibiotics
- use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics
- rapid diagnostic testing on blood specimens
- use of serial PCT measurements
- In patients with hematologic malignancy at risk of contracting invasive fungal disease (IFD), suggest incorporating nonculture-based fungal markers
- suggest monitoring antibiotic use as measured by days of therapy (DOTs) in preference to defined daily dose (DDD)
- measuring antibiotic costs based on prescriptions or administrations
- Include hem-onc units, antifungal stewardship, NICU and nursing homes

ACOG guideline for prevention and management of acute diarrhea

Am J Gastroenterol 2016 May 111:602

Salient features:

- In acute diarrhea (duration, 1–14 days), perform stool cultures and new culture-independent molecular assays (if available) when a patient is at high risk of spreading disease or during outbreaks.
- Consider stool diagnostic tests in presence of dysentery, moderate-to-severe disease, or symptom duration >7 days.
- Supplement traditional diagnostic stool tests (culture, microscopy with or without special stains, immunofluorescence, antigen testing), which are usually negative in acute diarrhea, with FDA-approved culture-independent molecular methods if available.
- Do not conduct antibiotic sensitivity testing in acute diarrhea.
- The use of a fecal leukocyte test or fecal lactoferrin to guide more appropriate use of cultures is "imprecise and probably unnecessary."
- With a few exceptions, most patients can adequately rehydrate with water, juice, sports drinks, soups, and salty crackers.

- Do not treat acute diarrhea with probiotics and prebiotics except for postantibiotic diarrhea.
- Treat mild-to-moderate traveler's diarrhea (TD) with bismuth subsalicylate except where contraindicated (e.g., use of other salicylates).
- Loperamide remains an excellent treatment for TD. Titrate the dose to avoid posttreatment constipation, and do not give for >48 hours. Loperamide may even be safe in a dysentery presentation that would increase the risk for an invasive pathogen, provided it is combined with antibiotic therapy.
- Do not conduct empiric antibiotic therapy in acute diarrheal infection, except in cases of TD in which a bacterial cause is deemed highly likely. Most community-acquired acute diarrhea is viral in origin.
- Treat TD with a single-dose or 3-day course of quinolones or single-dose azithromycin (1000 mg), except for suspected or cultured *Shigella*, which requires a 5-day course.

Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

Clin Infect Dis. first published online June 29 2016 doi: 10.1093/cid/ciw326

Answer to photo quiz

Axial T2-W MR image (Figure 1) shows symmetrical dentate nuclei hyper-intensities (dentate sign).

Only few pathologies are included in the differential diagnoses of bilateral dentate nuclei hyperintensities on T2-weighted MR images. These include methyl bromide intoxication, enteroviral encephalopathies, maple syrup urine disease and metronidazole toxicity. Among the anti-TB drugs, isoniazid & cycloserine have been reported to cause reversible bilateral dentate hyperintensities.

In the present case, the patient's medical history, temporal association of starting cycloserine and onset of symptoms and the results of clinical investigations (including CSF analysis) supported cycloserine as the etiology.

Cycloserine was discontinued. At follow-up, the patient remained asymptomatic. Repeat MR imaging of the brain eight weeks post discharge showed complete resolution of the bilateral dentate nucleus hyper intensities (Figure 2)

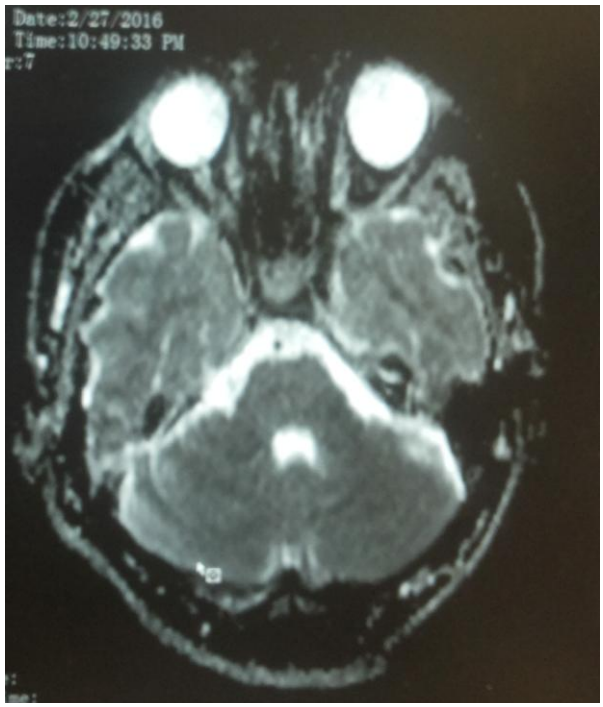

Figure 2: Complete resolution of the bilateral dentate nucleus hyper intensities

Final diagnosis: Cycloserine induced encephalopathy
(case provided by Dr Neha Gupta).


CIDS
CIDSCON - 2016
6th Annual Conference of
Clinical Infectious Diseases Society, India
Venue : Banaras Hindu University, Varanasi, Uttar Pardesh
Block your Dates
26th, 27th, 28th, August 2016
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