Volume 4, Issue 2

CIDS Newsletter

February 2017

CLINICAL INFECTIOUS DISEASES SOCIETY

Editor's note

Dear CIDS members

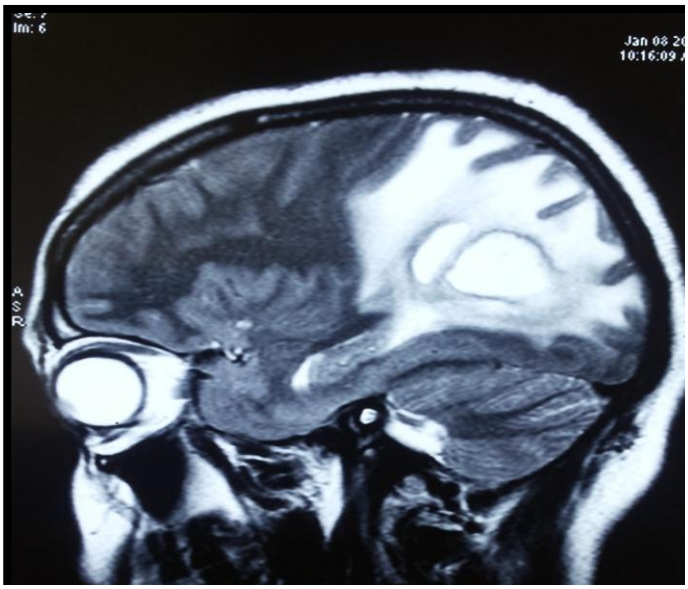
Please feel free to use the conference flyer in this newsletter in your talks and notice boards to publicize CIDSCON.

Sincerely

Ram Gopalakrishnan

Photo quiz

A 35-year old immunocompetent lady from a village in Uttar Pradesh presented in March 2015 with complaints of headache of 15 days duration. She had no history of fever, constitutional symptoms or seizures. There was no history of trauma or sinusitis. Investigations revealed a normal WBC count. MRI showed a ring-enhancing lesion in right parieto-occipital region (3.98 x 3.02 x 2.67 cm) suggestive of cerebral abscess which was reported as possible tubercular or pyogenic brain abscess **(Figure 1)**



What is your diagnosis?

Snippets from the literature

Rifampicin dose: higher the better?

(courtesy Dr Pratik Patil)
Lancet Infect Dis 2017; 17: 39–49

Pharmacokinetic studies indicate that standard dose (10mg/kg) of rifampicin often does not achieve effective plasma concentrations in patients. Newly diagnosed, rifampicin-sensitive, previously untreated pulmonary tuberculosis were randomly assigned in a 1:1:1:1:2 ratio to receive (all orally) either

- 35 mg/kg rifampicin per day with 15–20 mg/kg ethambutol,
- 20 mg/kg rifampicin per day with 400 mg moxifloxacin,
- 20 mg/kg rifampicin per day with 300 mg SQ109,
- 10 mg/kg rifampicin per day with 300 mg SQ109,
- or a daily standard control regimen (10 mg/kg rifampicin, 5 mg/kg isoniazid, 25 mg/kg pyrazinamide, and 15–20 mg/kg ethambutol).

Experimental treatments were given with oral 5 mg/kg isoniazid and 25 mg/kg pyrazinamide per day for 12 weeks, followed by 14 weeks of 5 mg/kg isoniazid and 10 mg/kg rifampicin per day. The primary endpoint was time to culture conversion in liquid media within 12 weeks. Recruitment was stopped early in the arms containing SQ109 since prespecified efficacy thresholds were not met at the planned interim analysis. Time to stable culture conversion in liquid media was faster in the 35 mg/kg rifampicin group than in the control group (median 48 days vs 62 days, adjusted hazard ratio 1·78; 95% CI 1·22–2·58, p=0·003), but not in other experimental arms. 45 (12%) of 365 patients reported grade 3–5 adverse events, with similar proportions in each arm.

A dose of 35 mg/kg rifampicin was safe, reduced the time to culture conversion in liquid media, and could be a promising component of future, shorter regimens. We can safely use higher doses, especially in patients with serious forms of TB such as TB meningitis or where absorption may be an issue.

Molecular rapid diagnostic tests for BSIs: worth it?

(courtesy Dr Pratik Patil)
Clin Infect Dis. (2017) 64 (1): 15-23

This meta-analysis found mortality risk was significantly lower with mRDT than with conventional microbiology methods [OR] 0.66, especially when combined with antimicrobial stewardship programs (ASPs) (OR, 0.64). The number needed to treat was 20 and time to effective therapy decreased by −5.03 hours and LOS decreased by −2.48 days.

The authors conclude that mRDT should be considered as part of the standard of care in patients with BSIs, provided stewardship is integrated into practice.

Late Relapse Versus Hepatitis C Virus Re-infection in Patients with Sustained Virologic Response After Sofosbuvir-Based Therapies

(courtesy Dr Amarjit Singh Vij)
Clin Infect Dis. (2017) 64 (1): 44-52.

The prevalence of late recurrent viremia (patients with SVR 12 weeks after the end of treatment but detectable HCV RNA at follow-up week 24) was investigated using refined phylogenetic analysis of multiple HCV genes to distinguish virologic relapse from re-infectionacross 11 phase 3 clinical trials of ledipasvir–sofosbuvir (SOF) and SOF. Only 12 of 3004 patients had detectable HCV RNA following SVR 12 weeks after the end of treatment. Of these 12 patients with late recurrent viremia, 11 had the same HCV genotype/subtype at baseline and at recurrence. Phylogenetic analysis demonstrated that 58% (7 of 12) of these patients were successfully treated with the SOF-based regimen, with HCV eradication achieved, but became re-infected with a different HCV strain after treatment. The remaining 5 patients with late recurrent viremia had virologic relapse in which the HCV present at baseline persisted in the liver or another compartment and reemerged in the blood 24 weeks after treatment. The incidence of late recurrent viremia was low.

Distinguishing reinfection from virologic relapse has implications for determining true treatment efficiency and selecting optimal retreatment strategies. To determine true treatment efficacy and define the most appropriate retreatment, it is important to distinguish virologic relapse from reinfection when patients in whom HCV is eradicated during treatment become infected with a new HCV strain after treatment.

And now resistance to both colistin and chlorhexidine?

(courtesy Dr Ashwini Chowdhary)
http://aac.asm.org/content/early/2016/10/12/AAC.01162-16.abstract

Here the authors investigated the mechanisms responsible and the phenotypic consequences for chlorhexidine adaptation with particular reference to antibiotic cross-resistance. In five of six strains adaptation to chlorhexidine also led to resistance to the last resort antibiotic colistin. Here we show that chlorhexidine adaptation is associated with mutations in the two component regulator *phoPQ* and a putative tet-repressor gene (*smvR*), adjacent to the MFS family efflux pump *smvA*. Up-regulation of *smvA* (10-27 fold) was confirmed in *smvR* mutant strains and this effect and the associated phenotype was suppressed when a wild type copy of *smvR* was introduced on plasmid pACYC. Up-regulation of *phoPQ* (5-15 fold) and *phoPQ*-regulated genes, *pmrD* (6-19 fold) and *pmrK* (18-64 fold), were confirmed in *phoPQ* mutant strains. In contrast, adaptation of *K. pneumoniae* to colistin did not result in increased chlorhexidine resistance despite the presence of mutations in *phoQ* and elevated *phoPQ*, *pmrD* and *pmrK* transcript levels. Insertion of a plasmid containing *phoPQ* from chlorhexidine adapted strains into wild-type *K. pneumoniae* resulted in elevated expression levels of *phoPQ*, *pmrD* and *pmrK* and increased resistance to colistin but not chlorhexidine. The potential risk of colistin resistance emerging in *K. pneumoniae* as a consequence of exposure to chlorhexidine has important clinical implications in infection prevention procedures.

Development of a Live Attenuated Bivalent Oral Vaccine Against Shigella sonnei Shigellosis and Typhoid Fever

(courtesy Dr Amarjit Singh Vij)
J Infect Dis (2016) 215 (2): 259-268.

Shigella sonnei and *Salmonella* Typhi cause significant morbidity and mortality. The safety record of the oral, attenuated *S.* Typhi vaccine (Ty21a) has been exploited by using it as a vector to develop a bivalent oral vaccine to protect against *S. sonnei* shigellosis and typhoid fever. The *S. sonnei*form I O-antigen gene cluster is recombineered into the Ty21a chromosome to create Ty21a-Ss, which stably expresses *S. sonnei* form I O antigen. To enhance survivability in the acid environment of the stomach, an acid-resistant strain, Ty21a-AR-Ss, by inserting *Shigella* glutaminase–glutamate decarboxylase systems coexpressed with *S. sonnei* form I O-antigen gene is created. Mice immunized intranasally with Ty21a-AR-Ss produced antibodies against *S. sonnei* and *S.* Typhi, and survived lethal intranasal *S. sonnei* challenge. This paves the way for proposed good manufacturing practices and clinical trials intended to test the clinical effectiveness of Ty21a-AR-Ss in protecting against *S. sonnei* shigellosis and typhoid fever, as compared with the current Ty21a vaccine.

Upcoming meetings and conferences

14th HISICON 2017 (XIV th National Conference of Hospital Infection Society India)

9th – 11th February 2017, Guwahati

www.hisicon.com

Answer to photo quiz

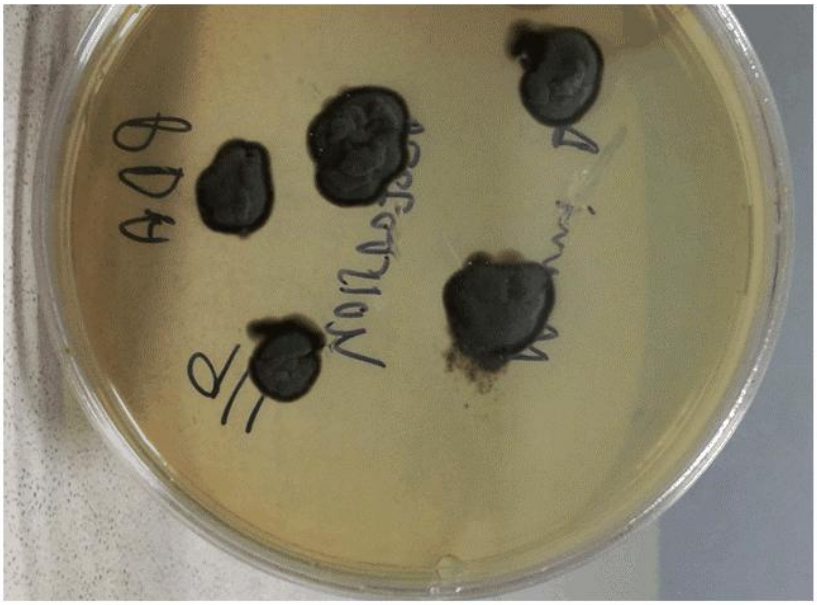


Figure 2: Fungal culture s/o *C. bantiana*

Cerebral brain abscess due to *Cladiophialophora bantiana*, a dematiaceous fungus, in an immunocompetent host is relatively rare. Cerebral phaeohyphomycosis must be considered in the differential diagnosis of mass lesions of brain, even in immunocompetent patients. Treatment options include complete surgical resection and effective source control with novel azole antifungals, such as voriconazole.

Following complete surgical debridement, patient was initiated on voriconazole treatment. Follow up at 3 months revealed clinical and radiological stability and voriconazole was discontinued. The patient is doing well at 1 year of follow up.

Final diagnosis: *Cladiophialophora bantiana* brain abscess

(case provided by Dr Neha Gupta)

CIDSCON 2017

7th Annual Conference of
Clinical Infectious Diseases Society, India

25th | 26th | 27th August, 2017

Venue : Le Méridien Nagpur, Maharashtra

Dr. V Ramasubramanian
Organizing Chairman

Dr. Ashwini Tayade
Organizing Secretary

Dr. O C Abraham
Scientific Committee Chairperson

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