Photoquiz

A 49/M with uncontrolled diabetes presented with fever (102-103), headache and subacute onset of left sided hemiparesis. There was no history of skin and soft tissue abscess. On examination, he had no dental caries, sinusitis or ear infection. Chest X-ray was normal with no evidence of consolidation or infiltrates. His complete blood count showed TLC of 16,000 with neutrophilic predominance and raised ESR (81). HIV ELISA was negative. CT scan showed a ring enhancing space occupying lesion (RESOL) (3.4 X 3.2 X 3.2 cm) in right thalamocapsular region with focal areas of cerebritis (Fig 1).

MR spectroscopy shows elevated lactate spikes (Fig 2)

What is your diagnosis?
IDSP country wide surveillance indicates that Cholera, Chikungunya, Chickenpox, diarrheal diseases followed by Dengue are the communicable diseases on the rise in early 2019 in India.
Zika virus in India

Contributed by Dr Veeren Ganta, Dr Ashwini Tayade

CDC issues Zika Warning for travellers to India

What can travelers do to prevent Zika?

- Pregnant women should NOT travel to areas with risk of Zika. This is because Zika infection during pregnancy can cause serious birth defects.

- All travelers to areas with risk of Zika should (1) prevent mosquito bites and (2) use condoms or not have sex to protect against Zika during travel. They should continue to take these precautions after their trip to stop the spread of Zika to others back home. See below for more information.

Microcephaly can't be ruled out in Rajasthan Zika outbreak

Contributed by Dr Veeren Ganta, Dr Ashwini Tayade

Pune-based National Institute of Virology (NIV) has come out with a study on strains of Zika virus (ZIKV) that led to an outbreak in Rajasthan in 2018, and in Gujarat and Tamil Nadu in 2016 and 2017 respectively.

- The NIV paper, to be published in ‘Infection, Genetics and Evolution’, said that mutation (S139N) leading to increased infectivity in humans causing microcephaly was not present, but “once ZIKV establishes in the Indian ecosystem, its chances of mutation (to other forms) cannot be neglected. Despite the absence of the proposed mutation on the transmission and microcephaly, the chances of not finding such a clinical condition cannot be guaranteed.”

- The paper further clarifies that a study done in Thailand by Wongsurawat et al. in 2018 found that despite the absence of this particular mutation, cases of microcephaly were reported. (Wongsurawat T, Athipanyasilp N, Jenjaroenpun P, Jun S, Kaewnapan B, Wassenaar TM, et al. Case of Microcephaly after Congenital Infection with Asian Lineage Zika Virus, Thailand. Emerg Infect Dis. 2018;24(9):1758-1761. https://dx.doi.org/10.3201/eid2409.180416)

- The paper also says that presence of the reverse mutation (N139S) can cause milder neurovirulence, that is, it can affect the nervous system. Yadav confirmed its presence in Indian ZIKV sequence retrieved from Rajasthan.

- More than 130 cases of Zika were reported in the last outbreak in Rajasthan, three in Gujarat and one in Tamil Nadu. More than 160 cases of Zika were reported in Madhya Pradesh as well.

- The study, therefore, confirmed that in all the three cases — Rajasthan, Gujarat and Tamil Nadu — it was Asian lineage at work, and not African. Asked if the former is more harmful than the latter, Yadav said, “Experimental studies need to be performed in order to comment on the extent of harmfulness of the Asian as well as African strain.”
Influenza H1N1 update - India

Contributed by Dr Veeren Ganta, Dr Ashwini Tayade

Source: https://www.promedmail.org/soas

As of 20th Feb, 2019, a total of 65 people succumbed to [influenza A] H1N1 virus in the country last week [week of 11 Feb 2019], pushing the death toll due to swine flu [influenza A(H1N1) virus] this year [2019] to 377, according to the Union Health Ministry, while the number of those infected by it has crossed 12,000.

- Rajasthan reported the highest number of cases (3508) and fatalities (127), the ministry data showed. Gujarat was placed 2nd on the list with 71 deaths and 1983 cases. In Delhi, 7 people died while 2278 people were infected by the virus. Punjab reported 31 deaths and 410 cases, followed by Madhya Pradesh 30 deaths and 128 cases. In Himachal Pradesh, 27 people died due to the virus and 224 were infected. Jammu and Kashmir reported 22 deaths and 293 cases; Maharashtra 17 deaths and 330 cases; and in Haryana, 7 people died while 752 people were affected.
- The data showed 12,191 people tested positive for H1N1 virus in the country this year till [17 Feb 2019]. Last year [2018], 14,992 cases and 1103 deaths due to the [influenza A/H1N1 virus] were reported.

JOURNAL REVIEW

OVIVA trial


Contributed by Dr Sowmya Sridharan, Dr Abi Manesh

Bone and joint infections typically are treated with a prolonged course (minimum of 6 weeks) of IV therapy followed by long term oral therapy. This is not based on rigorous data, rather from small studies done decades ago. OVIVA is a large RCT that explored whether oral therapy after the first one week will be as efficacious as 6 weeks parenteral therapy. The study was done in 26 sites in UK from 2010 to 2015. The study had a non inferiority margin of 7.5%. The primary outcome was treatment failure at 1 year follow up. The trial was done in a pragmatic fashion where all sorts of bone and joint infections including prosthetic joint infections were included.

Randomizing patients with an expected majority of gram-positive infections, there was no statistical difference in the rate of treatment failure between groups; IV with 14.6% compared to oral with 13.2% (95% CI -5.6 to 2.9). Probably or possible treatment failure was similar between groups along with rates of diarrhea associated with C. Diff and other adverse events. Therapy with IV antibiotics were associated with a longer hospital length of stay (14 days vs. 11 days, P < 0.001) with more early therapy discontinuation (18.9% vs. 12.8%, P = 0.006, NNH 16) and more IV catheter complications (9.4% vs. 1.0%, P < 0.001, NNH 12). The study had a small lost to follow up group (4%).

The result of the study is potentially practice changing. Concerns in this study include a higher rate of failures in both the groups and the authors have not reported on individual oral agents and their success rates. However, for most patients oral therapy could be used up front when agents with good oral bioavailability are available.
Mould infections in Indian ICUs

This important study gives information on mould infections from Indian ICUs- their epidemiology, presentations and outcomes. The authors studied 41879 subjects admitted in ICU at the 11 participating centres. In essence, they diagnosed definitive mould infection when there was histopathological evidence showing fungal hyphae and probable when there is indirect evidence (galactomannan positivity, culture or cytology showing fungal hyphae).

They concluded that there were 398 cases (proven 96, probable 302) of IMI amounting to a prevalence of 9.5 (range, 4.3-29.0) cases per 1000 ICU admissions. The classical (neutropenic patients and transplant hosts) and non-classical risk factor groups with IMI consisted of 145 (36.4%) and 253 (63.6%) of subjects, respectively. Lung and sinus involvement where the dominant presentation. Diabetes mellitus and lung diseases (influenza, COPD, asthma and interstitial lung diseases) were the dominant predisposing non classical risk factors. There were no specific radiological clues to suspect fungal infections in patients with non classical risk factors. Almost two third of patients with mould infections died. High APACHE II score and IMI due to mucormycosis were predictors of mortality after adjusting for the type of risk factor (classic vs. non-classic), the need for dialysis and the time from ICU admission to the diagnosis of IMI.

High clinical suspicion for mould infections in patients with non classical risk factors (DM and respiratory problems) may result in prompt treatment initiation and better outcomes.

Do you routinely colonize MRSA carriers

This pragmatic RCT evaluated the benefit of decolonisation along with hygiene education versus education alone in a diverse group of patients who have recently been discharged from the hospital. Participants were assigned in 1:1 ratio to receive either educational materials and proper hygiene (n= 1063) or educational materials plus decolonization routines (n= 1058), including the use of a 4% rinse-off chlorhexidine body wash, 0.12% chlorhexidine mouthwash (to be used twice daily), and 2% nasal mupirocin (to be used twice daily) twice monthly for 6 months. Of course, in view of the rigorous nature of the decolonisation regimen only two thirds could adhere to it.

Researchers found that 98 of 1058 patients (9.2%) in the education group and 67 of 1063 patients (6.3%) in the decolonization group had MRSA infection (HR, 0.70; 95% CI, 0.52 to 0.96; P=0.03 - ARR=0.029; NNT=34.5). Most of these infections are serious ones requiring hospitalisation. Pneumonia, surgical site infection and bacteremic infections were prevented preferentially. The mean duration between enrollment and development of infection in both the groups was about 4 months. The treatment benefit was stronger in the intention to treat group.

Though the event rates were low and treatment effect mild, this could be an useful intervention in select group of patients at high risk for MRSA infections as it prevented serious infections.
Impact of point-of-care C reactive protein on antibiotic prescriptions

BMJ Open. 2019 Feb 1;9(1):e025036
Contributed by Dr Abi Manesh

Point of care CRP and now procalcitonin are two markers which have a potential for "diagnostic stewardship" especially in primary and secondary care centres to decrease antibiotic use across various settings viz

1. Patients who present with febrile illness
2. Patients with respiratory illness
3. Patients with exacerbation of airway diseases like COPD.

Their positive effects have been documented in many RCTs, importantly among LMICs as well where the burden of AMR is high. In this systematic review, the authors evaluate the impact of POC CRP on antibiotic prescriptions. 11 randomised controlled trials and 8 non-randomised controlled studies and data from 16,064 patients were analysed in this review. All included studies had a high risk of performance and selection bias. Compared with usual care, point-of-care CRP reduced immediate antibiotic prescribing (pooled risk ratio 0.81; 95%CI 0.71 to 0.92), however, at considerable heterogeneity (I² =72%). This effect increased when guidance on antibiotic prescribing relative to the CRP level was provided (risk ratios of 0.68; 95%CI 0.63 to 0.74 in adults and 0.56; 95%CI 0.33 to 0.95 in children). They found no significant effect of point-of-care CRP testing on patient satisfaction, clinical recovery, re-consultation, further testing and hospital admission.

An important trial which also showed similar findings not included in the current review can be found here. In a high burden setting like India, point of care CRP can be an important adjunct to routine care to decrease antibiotic utilisation without compromising patient safety.
This prospective observational study puts forward a provocative argument. Many of us are aware that vancomycin being a clunky large molecule has poor tissue penetration especially in the lungs. We are also familiar with the RCT where linezolid bested vancomycin for nosocomial pneumonia. The authors studied children with MRSA pneumonia complicating flu over a 8 year period across 34 pediatric intensive care units from US. 170 children with severe flu requiring ICU admission were enrolled - of them 30 had MRSA pneumonia. Influenza-MRSA pneumonia was associated with increased leukopenia, acute lung injury, vasopressor use, extracorporeal life support, and mortality (P ≤ .0001). Influenza-related mortality was 40% with MRSA compared to 4.3% without (relative risk [RR], 9.3; 95% confidence interval [CI], 3.8-22.9).

Importantly, of 29/30 children with MRSA who received vancomycin within the first 24 hours of hospitalization, mortality was 12.5% (N = 2/16) if treatment also included a second anti-MRSA antibiotic compared to 69.2% (N = 9/13) with vancomycin monotherapy (RR, 5.5; 95% CI, 1.4, 21.3; P = .003). The following figure show the therapy used in the first 24 hours of treatment:

Age, gender, PRISM III score, type of influenza infection, and influenza vaccination did not significantly differ between the early vancomycin monotherapy and the additional early anti-MRSA antibiotic groups. The estimated number needed to treat with more than 1 anti-MRSA agent to prevent 1 death would be 2 (95% CI, 1.2, 3.7). This finding remained significant (P = .01) after adjusting for illness severity in the first 24 hours (PRISM III score) and age.

It may be that combination therapy, or an alternative agent altogether, represents a superior option for management of these high-risk patients.
CT guided drainage of the intracerebral lesion was performed and the pus culture grew α-haemolytic Streptococcus spp (Fig 3). With Pen E test, MIC was > 0.5 indicating a resistant streptococcus. According to the CLSI guidelines, Penicillin MIC is used for the guidance of the susceptibility of VGS in every possible case for appropriate treatment. There are no disc-diffusion criteria for VGS. Standard recommendations for treatment of ‘cryptogenic’ brain abscess are Vancomycin + Ceftriaxone + Metronidazole. As the patient had no risk factor for MRSA, empirical ceftriaxone 2 gm 12 hrly) and metronidazole 500 mg 6 hrly was initiated. Metronidazole was subsequently discontinued. IV ceftriaxone was continued which was shifted to oral cefixime subsequently.

Differential diagnosis of RESOL includes pyogenic brain abscess, tuberculoma, toxoplasmosis, tumor (astrocytoma, primary CNS lymphoma or metastasis), fungal abscess (Aspergillus, Mucor, Scedosporium) and nocardia.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Pyogenic brain abscess</th>
<th>Tuberculoma</th>
<th>Toxoplasmosis</th>
<th>Tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High grade fever, headache &amp; subacute onset FND</td>
<td>Fever usually low grade</td>
<td>Seropositive pt with seizures (35%) or FND</td>
<td>No fever &amp; not severe headache FND</td>
</tr>
<tr>
<td>WBC</td>
<td>WBC -16,000 N 71%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>Rt MCA territory with areas of cerebritis-haematogenous</td>
<td>Junction of grey white matter MC site-Basal ganglia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSF analysis</td>
<td>Neutrophilic leucocytosis</td>
<td>Lymphocytic predominance with high ADA</td>
<td>Unremarkable CSF s/o aseptic meningitis</td>
<td>RBC’s +++</td>
</tr>
<tr>
<td>MRI spectroscopy</td>
<td>Lactate peak +</td>
<td>Lipid peak decrease choline</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Final diagnosis**: Bacterial brain abscess caused by alpha hemolytic Streptococci (+- others)

*Case provided by: Dr Ranjit Sah, Dr Neha Gupta, Dr Rajeev Soman, Dr Anjali Shetty, Dr Camilla Rodrigues*