Corticosteroid Induced Cryptococcus Meningitis

Dear Editor,

Cryptococcosis is a disease of high morbidity and mortality, often presenting as meningitis in immunocompromised patients. Currently, acquired immunodeficiency syndrome is the most important predisposing factor in approximately 80-90% of cryptococcal infections. Cryptococcosis also occurs in patients, who are not infected with human immunodeficiency virus (HIV), like those who are on prolonged high dose or therapeutic dose corticosteroid therapy, patients with lymphoreticular malignancies as well as sarcoidosis even in the absence of corticosteroid therapy. We are reporting a case of cryptococcal meningitis in a HIV seronegative, 13 year old girl with autoimmune hemolytic anaemia for which she underwent longterm corticosteroid therapy.

Patient was admitted with acute symptoms of severe constricting type of headache, vomiting since 10 days and intermittent episodes of altered behaviour, seizures and fever of 7 days duration; the patient was admitted. She was a known case of autoimmune haemolytic anaemia or corticosteroid therapy (prednisolone- 4.5 mg/kg body weight/day) since one year. On examination, the child was febrile having exophthalmos, cushingoid facies, striae over legs and buttocks, erythema over face and enlarged posterior cervical lymph nodes. On central nervous system (CNS) examination, she was conscious with waxing and waning of sensorium, neck stiffness, upper motor neuron facial palsy, right twelfth cranial nerve palsy and generalized hypotonia. Reflexes could be just elicited. On examination cardiovascular system, respiratory and gastrointestinal systems were normal. Routine blood investigation revealed Hb - 4.2 gm%, TLC 5600/Cu.mm, DLC - N 80%, L 18%, and M 2%, ESR-50 mm/1st one hour. Her random blood glucose was 153 mg/dL. HIV ELISA was negative. Cerebrospinal fluid (CSF) analysis showed glucose-28 mg/dL, protein-30 mg/dL and no cells.

Microscopic examination of cerebrospinal fluid (CSF) by gram staining revealed gram positive budding yeast cells and India ink preparation demonstrated capsulated budding yeast cells. Culture of CSF on Sabouraud dextrose agar (SDA) grew mucoid yeast colonies after 72 hours of incubation at 37°C as well as 22°C which was identified as Cryptococcus neoformans by standard mycological techniques. The organism was not isolated in blood culture. Cryptococcus neoformans capsule polysaccharide antigen by latex agglutination test (Crypto-LA Test, Laboratories Fumouze) was detected in serum and CSF. In the diagnosis of cryptococcal meningitis, the patient was started on antifungal treatment with IV amphotericin B 600 mg/day for one week. Repeat CSF examination was positive for Cryptococcus neoformans both by culture and latex agglutination test (LAT).

The patient was given IV fluconazole 400 mg/day for three weeks. Patient showed clinical improvement, though LAT both for CSF and serum showed persistent positivity with a decline in antigen titre from 3+ to 1+. As her condition improved steadily, she was discharged with oral fluconazole 100 mg daily for 10 weeks. The patient was followed up for up to one year with review every 10 weeks. Even with one year of treatment with amphotericin B and fluconazole, LAT of serum and CSF persistently showed 1+ positivity as well as positive CSF culture, though the patient was symptom free.

Cryptococcus neoformans is recognized as the most frequent cause of fungal infection of the CNS in immunocompetent as well as in immunocompromised persons. Majority of the patients who develop cryptococcal meningitis are HIV seropositive. There are reports of cryptococcosis developing in HIV seronegative but immunocompromised. Host becomes vulnerable to cryptococcosis whenever there is defect in T cell mediated host defense mechanisms. In this case, prolonged corticosteroid therapy for the management of autoimmune haemolytic anaemia might have caused profound immunosuppression and predisposed for the development of cryptococcal meningitis.

A six week course of amphotericin B combined with flucytosine has been considered the treatment, of choice for cryptococcal meningitis with a good prognosis. In spite of adequate treatment, unlike in other reports, the blood and CSF examination remained positive both for cryptococcus antigen by LAT and CSF culture, even up to one year of follow up in our case, indicating necessity for prolonged treatment with antifungal drugs. Long term suppressive treatment, although not effective in preventing relapse, as it is seen in our case, may improve survival. This observation in our case also highlights the importance of periodic assessment of the immune status of the patients and subsequent modification of the management to prevent the development of cryptococcal meningitis.

References

Antibiotic Susceptibility Pattern and Plasmid Profile of Multidrug Resistant Salmonella typhi

Dear Editor,

Enteric fever continues to be a major health problem in India and plasmid mediated resistance in Salmonella typhi is known since 1972.1 Sixty three strains of S. typhi were isolated from blood and bone marrow cultures at the microbiology laboratory of Sri Ramachandra Medical College and Research Institute, Chennai, during the period, March 2002 to September 2002. Susceptibility to ampicillin, co-trimoxazole, chloramphenicol and Tetracycline (ACCOT) was determined by disc diffusion method. Minimal inhibitory concentration (MIC) to all the above drugs were determined by agar dilution method according to NCCLS standards using ATCC E.coli 25922 as control.2 ACCOT resistance was seen in 35 strains both by disc diffusion and MIC determination. The MIC values of the resistant strains were –ampicillin 2048 µg/mL, chloramphenicol 512 µg/mL, trimethoprim 160 µg/mL, sulfamethoxazole 128 µg/mL and tetracycline 1024 µg/mL. No resistance to ciprofloxacin, cefotaxime and ceftiraxone were observed by disc diffusion. However, the results have to be evaluated further by performing the MIC for these drugs. Also, these strains were subjected to alkaline lysis to isolate high molecular weight plasmid DNA and the plasmid was further analysed by restriction analysis. All the resistant strains carried a plasmid of 23 KB, and showed same restriction pattern with EcoR-I enzyme and Hind III enzyme. No plasmids were identified in the susceptible strains. ACCOT resistance is still common in S. typhi though declining with increased use of fluoroquinolones and cephalosporins for treatment.3 A continuous epidemiological surveillance is necessary and plasmid analysis is mandatory for studying the mechanism of drug resistance.

References


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