Multiple brain abscesses - diagnostic dilemma and therapeutic nightmare!

Sir,
A 32-year-old housewife presented with high-grade fever since 15 days, breathlessness, altered sensorium and seizures since 1 day, oozing right breast abscess since 2 months. There was no focal neurological deficit. Laboratory investigations revealed anemia, leukocytosis; HIV negative. Incision and drainage of the breast abscess was done. MRI brain showed multiple signal abnormalities in bilateral cerebellar hemispheres, pons, thalami, posterior limbs of internal capsule and left frontal sub cortical white matter [Figure 1] with peripheral ring enhancement post contrast. In view of the fever, seizures, breast abscess, the impression was multiple microabscesses in the brain. Pus culture of breast abscess was positive for klebsiella species. She was treated with intravenous antibiotics as per the sensitivity pattern (piperacillin-tazobactum), antiepileptics and supportive care for 4 weeks. She became afebrile after 2 weeks and was discharged after 4 weeks of treatment. However, after another 2 weeks she was readmitted with high grade fever, dyspnoea and maculopapular rash all over the body - Steven Johnson’s syndrome, secondary to phenytoin, hence it was changed over to levetiracetam. Her right breast abscess had healed completely. Hemoglobin and platelet count dropped, with leukocytosis and deranged liver and renal functions. She developed hypotension, oliguria, and acute respiratory distress syndrome (ARDS). 2 DECHO did not show any vegetation. Blood culture s/o MRSA coagulase positive staphylococcus aureus, procalcitonin level of 9.5; coagulation profile was suggestive of disseminated intravascular coagulation. She was put on inj imipenem-cilastatin (as per sensitivity), platelet and fresh frozen plasma transfusions, hemodialysis and supportive care.

She was investigated for vasculitis, tuberculosis, macrophage activation syndrome[1] (MAS) and toxoplasmosis, which were negative. Repeat MRI showed same ring enhancing lesions in left parietal, bilateral basal ganglia, pons, bilateral cerebellar hemispheres but with hemorrhagic changes with perifocal edema. Magnetic resonance spectroscopy [Figure 2] was done, which was suggestive of multiple brain abscesses with perifocal edema and hemorrhagic changes. Stereotactic biopsy of the lesion was deferred due to the hemorrhagic changes in
Letters to the Editor

Brain abscess is a focal intracerebral infection, beginning with a localized area of cerebritis and developing into a collection of pus surrounded by a well defined capsule. Seeding of the brain presumably occurs via transit of infecting bacteria through the valveless emissary veins that drain regions of paranasal sinuses, middle ear, teeth, etc., and permit direct or retrograde flow into the venous drainage systems of the brain. Other causes are penetrating injury, metastatic seeding of the brain from distant extracranial sources etc.\[^2\]\ In immunocompetent individuals the most common pathogens are *streptococcus* spp. (anaerobic, aerobic, and viridians-40%), *staphylococcus aureus*, enterobacteriaceae, proteus, klebsiella pneumonia and anaerobes. In immunocompromised hosts, it is mostly caused by *nocardia* spp, *aspergillus* spp, and *candida* spp.\[^1,3\]\ The incidence of multiple brain abscesses in all intracranial abscesses is about 2 to 15% and carry a mortality rate of 62 to 100%. Multiple brain abscesses are often caused by hematogenous spread of bacteria from a primary source and are frequently found in the territory of middle cerebral artery. Likely sources of primary infection include cyanotic heart disease, endocarditis, suppurative lung diseases, skin/abdominal and pelvic infections. They are common in patients with HIV infection, organ transplant recipients, intravenous drug abuse, chemotherapy for lymphoma, diabetes, congenital cardiac defects and prosthetic valves.\[^4\]\ Factors predictive of poor outcome include delay in diagnosis, choice of inappropriate antibiotics, ventriculitis due to rupture, bilateral/multiple, large, deep or multiloculated abscesses, posterior fossa abscesses, poor sensorium, hydrocephalus, septic shock, HIV co-infection.\[^1,3\]\ Our patient had bilateral, multiple brain abscesses in the posterior fossa, as well as supratentorial, a septic focus - untreated breast abscess, but no other risk factors. MRI, diffusion-weighted MRI, perfusion - weighted MRI also are sensitive methods for identifying cystic lesions and enhancement. Magnetic resonance spectroscopy study determines the concentration of brain metabolites such as N-acetyl aspartate, choline, creatine and lactate in the brain tissue, this technique helps in differentiating tumor from infective pathogens and abscesses.\[^5\]\ To summarize, our patient had multiple brain abscesses secondary to an untreated brain abscess and hematogenous spread. Her refractoriness to treatment and progressive deterioration led us to investigate her extensively. Though we could not get a tissue diagnosis, MR spectroscopy, a useful tool, aided and supported our diagnosis. Despite the availability of new antibiotics, new powerful imaging technologies and development of better neurosurgical techniques the therapeutic outcome of brain abscess has not shown a statistical significant change. Often, diagnostic challenge is stiffer than expected, and exact diagnosis may not be forthcoming even after clinical evaluation and a battery of tests, and besides the diagnostic dilemma, therapy can become a physician’s nightmare!

Kavita Krishna, Elizabeth Sada, Anita Vikram, Ankur Gupta
Department of Medicine, Bharati Vidyapeeth University Medical College and Bharati Hospital, Pune, Maharashtra, India

---

**Figure 1:** MRI brain showing multiple RELs in cerebellar hemispheres, pons, thalami, posterior limbs of internal capsule and left frontal subcortical white matter

**Figure 2:** MR spectroscopy showing a subcortical brain abscess with hemorrhagic changes; aminoacid, acetate and succinate peaks were observed
Letters to the Editor

Sir,

At the outset let me thank and congratulate the authors Obulesu M and Rao DM for compiling a much-needed review on the beneficial role of plants/plant extracts in managing the burgeoning and devastating problem of Alzheimer's disease (AD).

To date, four cholinesterase inhibitors or ChEI (tacrine, rivastigmine, donepezil and galantamine) and a partial NMDA receptor antagonist (memantine) are the only approved treatment options for AD. However, these drugs fail to completely cure the disease, which warrants a search for newer class of targets that would eventually lead to effective drugs for the treatment of AD. This is pertinent and timely information for researches in this field as existing therapies in the field, which are limited in number, have shown disappointing results. As pointed out by the author's "Plants provide wealth of bioactive compounds, which exert a substantial strategy for the treatment of neurological disorders such as Alzheimer's disease."[1]

It would be worthwhile to include certain additional plants of Indian origin that have demonstrated to possess beneficial properties for managing dementia/AD. Notable among them is "Aged Garlic Extract" (AGE) and one of its active ingredients, S-allyl-L-cysteine (SAC), which has demonstrated to restrict several pathological cascades related to the synaptic degeneration and neuroinflammatory pathways associated with AD.[2]

It was demonstrated that mice treated with pomegranate juice had significantly less (approximately 50%) accumulation of soluble Abeta42 and amyloid deposition in the hippocampus as compared to control mice. However, further studies to validate and determine the mechanism of these effects, as well as whether substances in pomegranate juice may be useful in AD, should be considered.[3]

Study also indicates Murraya koenigii (Curry leaf) to be a useful remedy in the management of Alzheimer's disease and dementia.[4]

Daucus carota extract (carrot) reversed the amnesia induced by scopolamine and diazepam besides significantly reducing the brain acetylcholinesterase activity. Therefore, Daucus carota extract may prove to be a useful remedy for the management of cognitive dysfunctions.[5]

There is evidence demonstrating the promising role of saffron (Crocus sativus) in the management of patients with AD. These naturally occurring agents in the diet have great potential, thus proving Hippocrates, who proclaimed 25 centuries ago, "Let food be thy medicine and medicine be thy food." Given the fact that most of the above-mentioned plants are consumed regularly in the diet, their incorporation could be feasible even in many distant and rural areas of our resource-constrained country. These treatment avenues can reduce treatment gap especially to the underprivileged and deprived patients residing in rural isolated areas of our developing countries with lowest conceivable affordability.

Given intense clinical need and carer concerns that lead to exploration of such alternatives as herbal medicines, research priorities should be aimed at establishing an ongoing authoritative database on herbal medicine for dementia. Further epidemiological and follow-up studies are required to determine the efficacy, safety, and mechanisms of action of these natural compounds in the treatment of AD.

References