CASE REPORT

An unusual cause for rings in the brain

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We report the case of a 35-year-old man from North India who presented with generalised tonic-clonic seizures and was found to have ring-enhancing brain lesions. He had a coincident adrenal mass lesion. Cultures from both regions grew *Histoplasma capsulatum*. He improved on treatment with itraconazole. This case is being reported since cerebral ring-enhancing lesions are rarely associated with histoplasmosis, and coincident adrenal involvement is also a rarity in an immunocompetent individual.

Case report

A 35-year-old unemployed man from West Bengal in North India presented to us in September 2010 after a single episode of generalised tonic-clonic seizures followed by loss of consciousness for 20 minutes. Following this, he developed bilateral lateral rectus palsies, a left upper motor neuron facial palsy, paresis of the left upper and lower limbs with grade-4 power, and exaggerated deep tendon reflexes. Higher mental functions were normal, however. His serum sodium level was 123 (reference range, 136-144) mmol/L and potassium level 4.0 (reference range, 3.5-5.0) mmol/L. His blood glucose levels, chest X-ray, and erythrocyte sedimentation rate were normal. Contrast-enhanced brain computed tomography (CT) showed multiple ring-enhancing lesions in the right parietal (Fig 1), right midbrain, and pontine regions. A routine ultrasonogram of the abdomen revealed a left suprarenal mass, which was confirmed by CT of the abdomen.

A CT-guided biopsy of the adrenal mass revealed necrotic material with no viable areas. Stereotactic-guided craniotomy and total excision of the right parietal lesion was performed. The biopsy specimens showed necrotising granulomatous inflammation and occasional small spherical structures resembling histoplasma, when stained by Periodic Acid Schiff with diastase. Both the adrenal and brain biopsy samples yielded *Histoplasma capsulatum* on culture (Fig 2).

This patient was not immunocompromised and serology for human immunodeficiency virus was negative. He did not have any history suggestive of a deficient cellular immunity. His absolute lymphocyte count was normal. He denied involvement with recreational activities that could have predisposed him for *Histoplasma* infection, or exposure to bat or bird droppings. He was started on oral itraconazole 200 mg twice daily as he did not have resources to take the liposomal or deoxycholate forms of amphotericin. He was also started on dexamethasone as an anti–cerebral oedema measure. As the random serum cortisol in the sample drawn prior to starting glucocorticoids was inappropriately low for the level of stress and hyponatraemia in the patient, he was switched to a maintenance dosage of prednisolone after dexamethasone was tapered off. An objective assessment of the adrenal reserve was not tested, as glucocorticoids had already been administered. Reassessment of the adrenal axis was deemed indicated after glucocorticoid therapy ceased.

The patient's condition improved on treatment. The right lateral rectus palsy resolved and the left upper limb power returned to normal. He remained seizure-free on 300 mg of phenytoin daily. On review after 9 months of treatment with itraconazole, the lesions in the brain showed significant resolution.

Discussion

Histoplasmosis is an infectious disease caused by the dimorphic fungus *H capsulatum*.[1] Infection develops when *Histoplasma* microconidia are inhaled into the lungs, where they change into yeast forms. Neutrophils, macrophages, lymphocytes, and natural killer cells are attracted to the sites in response to the infection. Macrophages assist in spreading the organism via lymphatics and the blood to the adjacent lymph nodes and throughout the reticuloendothelial system (liver, spleen, lymph nodes, adrenal glands, and bone marrow).

Key word
Histoplasmosis

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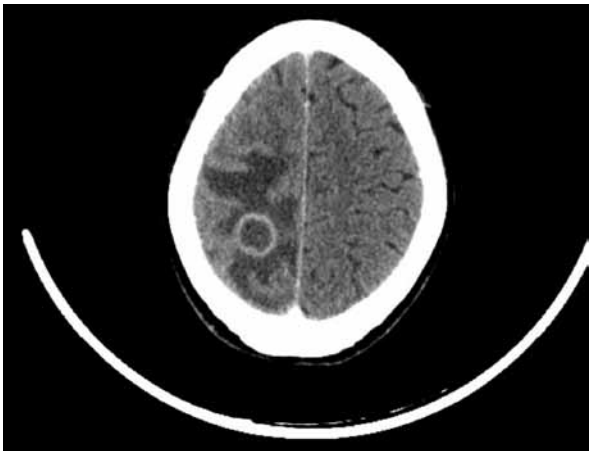

FIG 1. Computed tomography of the brain showing a ring-enhancing lesion with perilesional oedema in the right parietal region

罕見病因引致的腦部環形強化病灶

本文報告一名居住在印度北部的35歲男性，他有全身性強直—陣攣發作。檢查報告顯示腦部環形強化病灶。病人同時有腎上腺腫塊，細胞培養發現有莢膜組織胞漿菌。病人服用伊曲康唑（itraconazole）後病情有改善。本病例的特點是腦部環形強化病灶很少與組織漿菌症有關，且同時間牽涉腎上腺，這對於一個具免疫力的人來說是很罕見的。

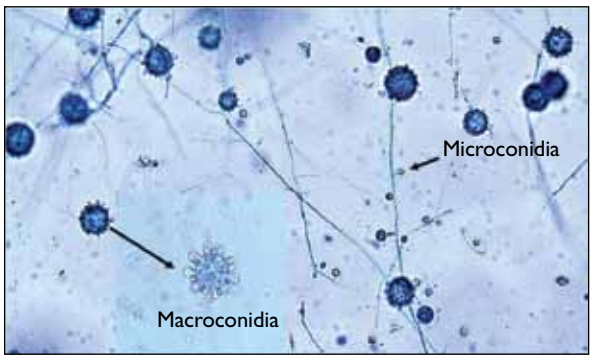

FIG 2. Characteristic 'sunflowers in bloom' appearance of macroconidia of *Histoplasma capsulatum*; microconidia are also seen (lactophenol cotton blue preparation, x 400)

In immunocompetent persons, asymptomatic lung impairment ensues but usually resolves without treatment.[2] Adrenal involvement is common (80-90% of autopsied cases), but overt adrenal insufficiency ensues in less than 10% of cases.[3] Adrenal involvement in disseminated histoplasmosis is usually bilateral. However, unilateral mass lesions are also described.[4] The adrenal sinusoids may be diffusely involved, or there may be focal collections of parasitised macrophages in the medulla, zona reticularis of the cortex, or corticomedullary junction. Adrenal insufficiency occurs from perivasculitis leading to thrombosis and infarction of the gland.

Central nervous system involvement occurs in 5 to 20% of cases of disseminated histoplasmosis and is more common in those with underlying immunosuppressive disorders.[5,6] Disseminated histoplasmosis, especially a ring-enhancing brain lesion, is uncommon in an immunocompetent adult.[7] Tuberculosis would have been the more obvious diagnosis in our case, but brain biopsy and cultures established the presence of histoplasmosis. Amphotericin B followed by oral azoles is the classically described treatment.[8] However, the lesser nephrotoxicity and oral route for administering azoles is a clear advantage over amphotericin. Itraconazole is insoluble in water, is strongly protein-bound, and has high and sustained tissue penetration. Central nervous system penetration of azoles increases in the presence of inflammation. The clinical response to treatment justified use of this drug in our patient. With such a dramatic response along with earlier reports,[9] an azole is worth considering as an acceptable alternative to amphotericin B, particularly in resource-poor settings.

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