Commentary: Ocular histoplasmosis and nocardiosis co-infection: A rare presentation

Systemic histoplasmosis is ubiquitous, and the causative fungus is found in the soil fertilized by birds, chicken, and bats.[1-4] Histoplasmosis is common in immunosuppressed individuals and may present with mild influenza, which often leads to granulomatous disease and can even progress to life-threatening disease.[1-4] In developing countries such as India, it can mimic tuberculosis.[3,4] Ocular manifestations of systemic histoplasmosis include retinitis, choroiditis, optic neuritis, uveitis, and endophthalmitis.[1-4] Presumed ocular histoplasmosis syndrome (POHS) may present with peripheral retinal or choroidal involvement called "histo spots," and they mostly have clear vitreous, unlike systemic histoplasmosis.[1,2] POHS is mostly immunologic. Choroidal neovascular membrane is a known complication of histo spots in POHS.[1,2]

Nocardia, on the other hand, is a bacterial infection that causes invasive disease involving skin, eyes, and lungs.[5,6] Every bodily organ can be affected by *Nocardia*.[5-9] Several studies conducted in southern India on *Nocardia* keratitis have found that initial diagnosis can be easily missed and delayed diagnoses were commonly encountered in these studies.[6,7] Studies from Hyderabad, India have concluded that *Nocardia* keratitis constitutes 1.7% of all bacterial keratitis cases.[6,7] *Nocardia* keratitis has a characteristic appearance on slit-lamp examination.[6,7] Punctate epithelial erosions and anterior corneal stromal infiltrates are seen in wreath patterned appearance with adjoining satellite lesions.[6,7] Infiltrates can also be found in the mid-periphery of cornea.[6,7] *Nocardia* scleritis and endophthalmitis have also been reported in literature.[6-9] *Nocardia* is a Gram-positive, aerobic organism found in soil and infection is usually exogenous.[5-9] They are weak acid-fast bacilli and can be picked up by Kinyoun's acid-fast staining as well. Arial hyphae are also seen.[8,9]

In the present article, a rare case of co-infection of histoplasmosis and *Nocardia* has been presented in a 48-year-old Indian man who was immunocompromised.[1] The patient presented with a conjunctival mass in the right eye and on histopathology, encapsulated bodies with bloated macrophages were observed, suggesting diagnosis of histoplasmosis.[1] Patient had past history of using systemic immunosuppressants and was taking oral steroids and tablet tacrolimus.[1] He had renal transplantation previously for mesangioproliferative glomerulonephritis.[1] Additionally, he had history of fever, cough, and multiple abscesses on thigh with discharging sinuses. Computed tomography of thorax revealed bilateral lung nocardiosis.[1] Cerebral abscess was also noted on imaging.[1] Fine-needle aspiration cytology of lung nodule and thigh abscess revealed *Nocardia farcinica* infection, for which he was treated with systemic antibiotics and regulation of immunosuppressives.[1] Local amphotericin 0.15% eye drop was prescribed in the postoperative period for the right eye.[1]

This dual infection in an immunocompromised, post-renal transplant patient was a challenge as systemic antifungal medications could lead to a compromised kidney function.[1] Systemic infection by *Nocardia* with foci in lung, brain, and thigh complicated the situation further. In metastatic nocardiosis, antibiotics have to be added by the concerned physician/internist for the best possible management. Cotrimoxazole sometimes work best in such a situation.[1] At the same time, baseline immunosuppressives have to be continued in the patient.[1] In such a situation, it is advisable for the patient to be admitted in the hospital.[1] The author (s) could have provided detailed neurological and complete systemic work-up. Consideration to include concerned specialists for such complicated cases should also be kept in mind for the best possible management.[1]

As new infectious diseases are emerging, they continue to be among the leading causes of mortality.[10] Medical management and drug resistance have increased

tremendously in the last decade. Monitoring and evaluation under the supervision of the Global Outbreak Alert and Response Network (GOARN)[10] for containment of various infections has come into existence.[10] Advances have been made in microbial detection and susceptibility systems.[10] Molecular methods are useful in situations where conventional methods fail to diagnose the causative organisms.[10]

It is a natural query for all of us that why there are multiple infections in immunosuppressed individuals. As in host cells, defense mechanisms are altered by CD4 cells, which are seen more in infected cases with human immunodeficiency virus (HIV) involvement.[10] Follicular cells from the lymphoid tissue become susceptible to the infection even without involving CD4 cells, particularly in exogenous infections affecting skin, cornea, and so on. Lymphopenia, selective T-cell deficiency, decreased delayed hypersensitivity reaction on skin test, hypergammaglobulinemia (IgG, IgA, and IgM), and polyclonal activation of B cells can induce such infections. Majority of *Nocardia* species have mycolic acid in their cell wall and trehalose 6-6′ dimycolate, a cord factor which is important for virulence.[5,6] The cord factor has been found to be interlacing with phagocytosis, by various macrophages in the lysosomes.[5,6]

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