ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 3, Issue – 6, November - 2018, Page No. : 48 - 52

Disseminated cutaneous rhinosporidiosis presenting as IRIS in a patient on treatment with HAART –Case report and review of literature

Sheela Mathew, Supriya PS, Aravind R

Department of Infectious Diseases, Govt. Medical College, Trivandrum, Kerala, India

Corresponding Author: Sheela Mathew, Department of Infectious Diseases Govt. Medical College, Trivandrum, Kerala, India

Type of Publication: Case Report

Conflicts of Interest: Nil

Abstract

The immune reconstitution inflammatory syndrome (IRIS) in HIV-infected patients initiating antiretroviral therapy (ART) results from restored immunity to specific infectious or non-infectious antigens. It may be either paradoxical clinical worsening of a known condition or the appearance of a new condition after initiating therapy. Potential mechanisms for the syndrome include a partial recovery of the immune system or exuberant host immunological responses to antigenic stimuli. Here we report a case of disseminated cutaneous rhinosporidiosis presenting as IRIS in a patient on treatment with ART for HIV associated AIDS

Keywords: Rhinosporidiosis, immune mechanisms, IRIS, HIV

Case report

47 yr old male presented with swelling forehead which was bleeding to touch. He was evaluated for excision biopsy and found to have HIV infection also. His CD4 count was 228/cu.mm. The differential diagnoses considered were Molluscum contagiosum, pyogenic granuloma and Kaposi's sarcoma. Excision biopsy was done. Biopsy showed thick walled spherical sporangia of varying sizes containing endospores and many free lying endospores suggestive of rhinosporidiosis.(Fig 1-3)

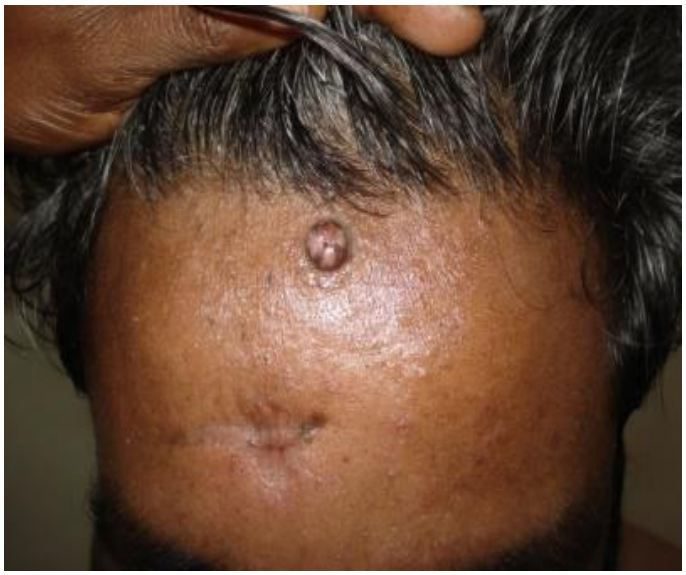

Figure 1 : Nodule forehead

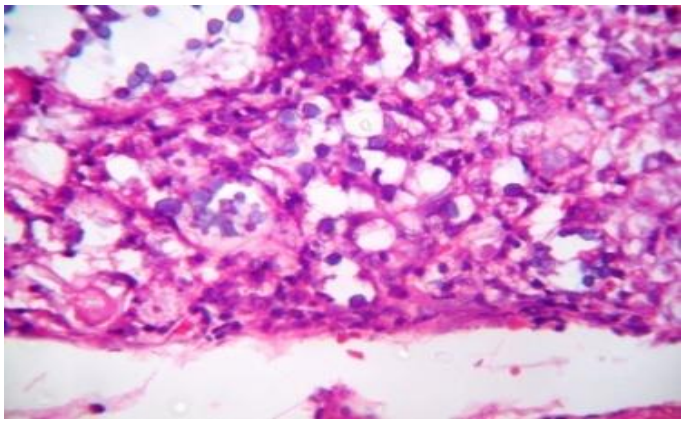

Figure 2:

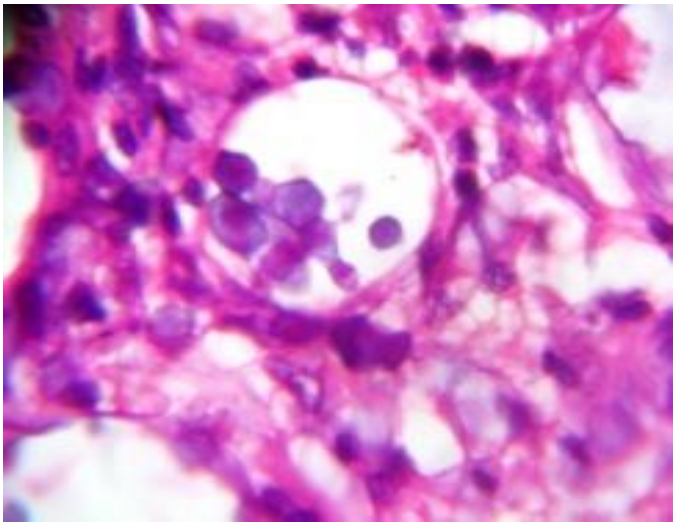

Figure 3:

Figure 2 and 3: H&E stain showing sporangia.

On repeated questioning, he gave history of removal of swelling nose 12yrs back for epistaxis. After that he was asymptomatic and no details of previous surgery were available. He was started on ART. One month later he reported development of a single nodule over back of chest and subsequently several swellings over different parts of body. Along with it there were subcutaneous swellings over forearm and scalp (Fig 4-6). Cutaneous swellings were mimicking Molluscum contagiosum, but because of the occurrence subcutaneous swellings FNAC was done from cutaneous and sub cutaneous swellings. The smear showed numerous spores scattered singly and in tiny clusters and sporangia in a back ground of lymphocytes, blood and macrophages suggestive of rhinosporidiosis (Fig 7-8).

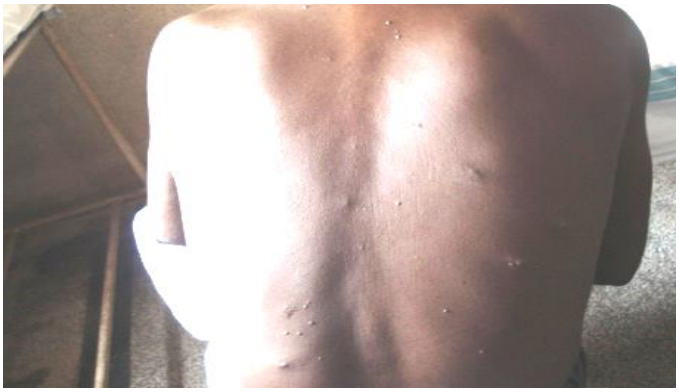

Figure 3: Multiplenodules

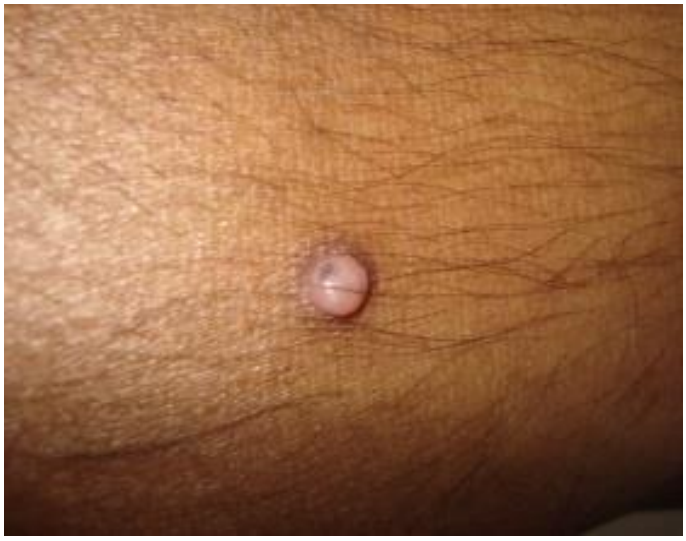

Figure 4: Nodules resembling molluscum

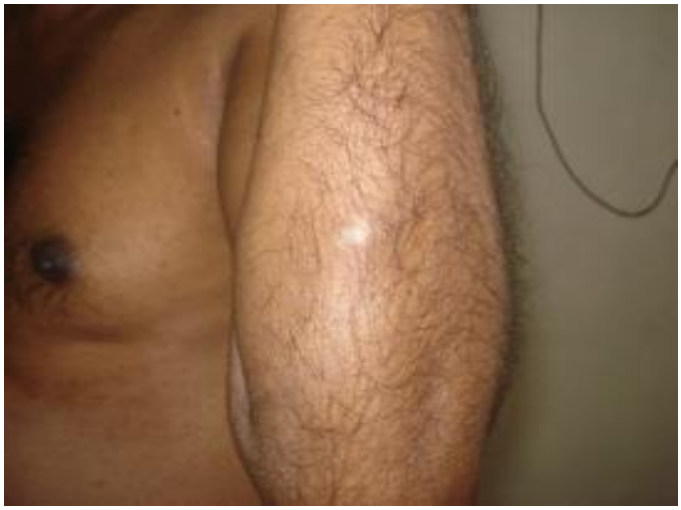

Figure 5: Sub cutaneous nodule

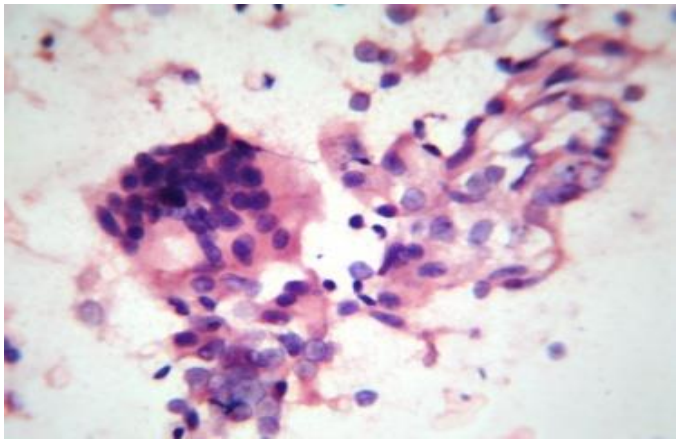

Figure 7:

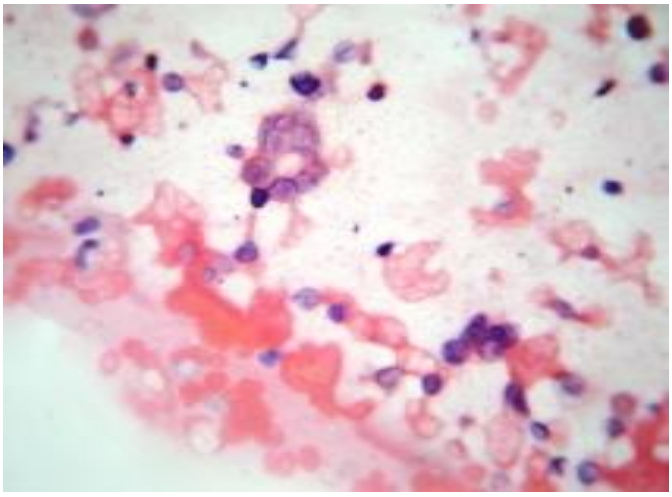

Figure 8:

Figure 6 & 8 pap stain showing multinucleated giant cell (arrow), endospores & sporangium (arrow)

Treatment with Dapsone was started. After 3 months of HAART, CD4 was repeated and it was 296/cu.mm. Here the patient presented with single swelling forehead, soon after starting HAART developed multiple swellings of same pathology and associated with rise in CD4 count suggesting IRIS.

Discussion

Immune reconstitution inflammatory syndrome in AIDS is the overwhelming inflammatory response of the body to previously acquired infectious or non-infectious antigens that paradoxically makes the symptoms worse when the immune system of the body recovers. There are two presentations. It may be either paradoxical clinical worsening of a known condition or the appearance of a new condition after initiating therapy.

Following ART an increase in memory CD4 cell types is observed possibly as a result of redistribution from peripheral lymphoid tissue (1)**.** This CD4 phenotype is primed to recognize previous antigenic stimuli, and thus may be responsible for manifestations of IRIS seen soon after ART initiation. After this redistribution, naïve T cells increase and are thought to be responsible for the later quantitative increase in CD4 cell counts. These data suggest IRIS may be due to a combination of both quantitative restoration of immunity as well as qualitative function and phenotypic expression observed soon after the initiation of ART. These pathogenic mechanisms may interact and likely depend on the underlying burden of infectious or noninfectious agent.

The infectious pathogens most frequently implicated in the syndrome are Mycobacteria, Varicella zoster, Herpes viruses, Cytomegalovirus (CMV), Pneumocystis Pneumonia, Cerebral Toxoplasmosis, Isosporiasis, Cryptococcal Meningitis etc(2).

Rhinosporidiosis is a chronic disease of humans and other animals caused by *Rhinosporidium seeberi*. The disease is characterized by the formation of polyps primarily on the mucus membranes of infected hosts. Rhinosporidiosis has been reported from about 70 countries with diverse geographical features although the highest incidence has been from India and Sri Lanka. The presumed mode of infection from the natural aquatic habitat of *R.seeberi*, is through the traumatized epithelium (‘transepithelial infection’) most commonly in nasal sites. *R.seeberi* had first been regarded as a sporozoan by Malbran, its discoverer, in 1892, as a protozoan by Seeber who first published a description of the pathogen and then, as a phycomycete by Ashworth in 1923 (3). Through molecular biological analysis of the organism’s ribosomal DNA, Herr *et al* (4) classified the organism in a new clade which was named the *Mesomycetozoa*

The organism initiates it’s in vivo cycle with the entry of endospores into the host's mucosal membranes. Once implanted, the endospores differentiate by stages into juvenile, intermediate, and mature sporangia. The maturing sporangia undergo nuclear division and progressive cytoplasmic cleavage giving rise to numerous endospores which may number 16000 to 20000 per sporangium. When the endospores are released, the in

vivo life cycle is reinitiated. Rhinosporidiosis is an infection that is typically limited to the mucosal epithelium. Infection usually results from a local traumatic inoculation with the organism. The disease progresses with the local replication of *R seeberi* and associated hyperplastic growth of host tissue and a localized immune response (5). Infection of the nose and nasopharynx is observed in 70% of persons with rhinosporidiosis; infection of the palpebral conjunctivae or associated structures (including the lachrymal apparatus) is observed in 15%. Other structures of the mouth and upper airway may be sites of disease. Disease of the skin, ear, genitals, and rectum has also been described. Genital disease has been described in the vagina, penile urethra or meatus, and scrotum.

Mode of spread

Three different modes of spread have been postulated by Arseculeratne (6). The phenomenon of satellite lesions adjacent to granulomas especially in upper respiratory sites favors autoinoculation. Spillage of endospores from polyps after trauma or surgery is thought to be due to auto inoculations. Appearance of fresh lesions in anatomically distant sites like subcutaneous granuloma in limbs without any skin breach is explained by heamatogenous dissemination. Ashworth suggested possibility of lymphatic spread but not convincingly proved (3).

Mechanism of immunity

In spite of presence of high titer of anti rhinosporidial antibody, the disease exhibits chronicity, recurrence and dissemination. In vitro studies have shown such antibodies do not cause metabolic inactivation or morphological damage in endospores of *Rhinosporidium seeberi* indicating such antibody is ineffective in vivo.

Cell mediated immune response was demonstrated by assay of lympho proliferative responses to rhinosporidial antigens and the T cell mitogen Concanavalin A of peripheral blood lymphocytes of patients with rhinosporidiosis and by the foot pad delayed type hyper sensitivity responses to rhinosporidial antigens in experimental mice(7). Further, mouse experiments have shown that repeated sensitization with rhinosporidial antigen, the DTH foot pad response decreased significantly in intensity. The repeated exposure causes stimulation of CD4 Th-0 cells to production of CD4 positive Th-2 cells after an initial production of Th-1 cells. The Th-1 cells induce delayed type hypersensitivity while Th-2 cells encourage antibody production. Thus there is decrease in cell mediated immunity which may explain chronicity, recurrence, and dissemination of rhinosporidiosis.

Dapsone is the only drug having some anti-rhinosporidial effect which arrests maturation of sporangia and promotes fibrosis in stroma, when used as an adjunct to surgery.

Conclusion

The specific restoration of defective immune function offers significant promise in treating and preventing infections in immunocompromised patients. However the same intervention may also result in unexpected worsening symptoms of infection. This observation has been frequently observed in patients with AIDS, who undergo immune recovery in response to HAART. With increased immune system function these patients can paradoxically develop symptomatic infections with various pathogens presumably due to a reawakening immune system that is now able to respond to present pathogens.

References

1. Autran B, Carcelain G, Li TS, Blanc C, Mathez D, Tubiana R, Katlama C, Debre P, Leibowitch J: Positive effects of combined antiretroviral therapy on CD4+ T cell homeostasis and function in advanced HIV disease. *Science* 1997, 277(5322):112-116

2. David M Murdoch,Willem DF Venter,Annelies Van Rieand Charles Feldman Immune reconstitution inflammatory syndrome (IRIS): review of common infectious manifestations and treatment options *AIDS Research and Therapy* 2007

3. Ashworth JH. On *Rhinosporidium seeberi* (Wernicke, 1903) with special reference to its sporulation and affinities. *Trans Roy Soc, Edin* 1923; 53:301-342

4. Herr RA, Ajello L, Taylor JW, Arseculeratne SN,Mendoza L. Phylogenetic analysis of *Rhinosporidium seeberi'*s 18S Small-subunit Ribosomal DNA groups this pathogen among members of the Protoctistan Mesomycetozoa clade. *J clin microbiol* 1999;37(9):2750-2754.

5. Karunaratne WAE. The pathology of rhinosporidiosis. *J Path Bact* 1934;XLII:193-202.

6. Arseculeratne SN .Recent advances in Rhinosporidiosis and *R. seeberi* Indian journal of Medical Microbiology, (2002) 20 (3):119-131

7. Arseculeratne SN ,Atapattu DN, Eriyagama NB Human anti rhinosporidial antibody does not cause metabolic inactivation or morphological damage in endospores of *Rhinosporidium seeberi* Indian journal of Medical Microbiology, (2005) 23 (1):14 -19