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NANNIZZIOPSIS SPECIES OF FUNGAL DISEASE IN COVID PATIENTS

[1]M. Prasanthi [*], [2]Sk. Shabana Azmi ,

*Assistant professor of Department of Pharmaceutical Analysis,Nirmala college of Pharmacy, Acharaya Nagarjuna University, Atmakur, 522503, Andhra Pradesh, India.

*Corresponding author:

Department of Pharmaceutical Analysis,
Nirmala College of Pharmacy,
Acharaya Nagarjuna University,
Atmakur, Mangalagiri 522503, Andhra Pradesh , India.E-mail address: shabana098sk@gmail.com
Tel: + 8341050180; Fax: + 8341050180

ABSTRACT:

As the whole world battles the COVID pandemic, where in India besides its twisted off-springs the Black and White fungus wreaking havoc, now the first case of yellow fungus has also reported from Ghaziabad in Uttar Pradesh by ENT specialist. Yellow fungus is considered to be more dangerous than Black and White fungus. While black fungus epidemic in some states, yellow fungus isn't exactly new. A yellow fungus infections, which is scientifically known as Nannizziopsis species. These are much like other fungal infection spreads via contaminated environments, or when a suspected patient inhales moulds (mycomycetes) which grow in environment.This fungus infection starts to cause symptoms by launching an attack on the body's internal organ, and disturbing vital bodily processes.As this disease going viral and being pandemic in COVID situation every citizen should be aware of this disease from being complicated to humanlife. The present review draws a complete image of epidemiology, morphology, taxonomy, cultural characteristics, pathogenesis, case studies, risk of causing, symptoms and discussion.

KEY WORDS:

COVID, yellow fungus, Mycomycetes, Nannizziopsis species, Fungal infections,Chrysosporium Anamorph.

INTRODUCTION:

Yellow fungus is scientifically known as Nannizziopsis Vriesii which is a keratinophilic microfungus in the family Onygenaceae of the order Onygenales. It also includes in this family are dermatophytes and saprophytic species[1] . while the ecology of N.Vriesii is not well known,there has been several studies which identifies the Chrysosporium anamorph of N.Vriesii as a casual agent of skin lesions in reptiles across several regions[2] . This species is usually identifiedunder microscope by its white ascomata, and hyaline and globose **ASCOSPORES**[3] . Now it is transmitted to humans in inhale process and entering the body's internal organ and leading to the damage.

MORPHOLOGY:

Like many other fungi, N. vriesii has sexual and asexual state, the asexual states are classified as the genus Chryososporium, Malbranchea or Sporendonema. The Sexual stage of N. vriesii consists of a whitish tumble-weed like fruiting body which is approximately 1mm in a diameter and a central cluster of asci containing ascospores[1]. The hyphae which consist of exterior fruiting bodies, are chacteristically rough-walled with septal constrictions. The lens shaped ascopores are brown in color and range in size from 2-3μm^3. Like other members in the family Onygenacae, N. vriesii produces rhexolytically dehiscing conidia.[1] which can be either teadrop shaped or club-shaped, and form directly on the sides of hyphae.[5]

TAXONOMY:

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N.vreisii was first described under the genus Rollandina by Patouillrad in 1905. In 1970, further studies by Benamin and Apinis lead to the several new species, including R. vriesii to the genus Rollandina.[4]Rollandina vreisii was placed under family Rollanda because the result of morphological studies demonstrated that its hyphae was similar to species previously described by Patouillard's.[1]Rollandina vriesii was classified in the family Onygenaceae because its ability to degrade keratin as demonstratedby hair perforation, and the presence of spheroidal ascopores with punctuate walls.[1] This was later classified under the genus Nannizziopsis which was first believed to be synonymous to the genus Arachnotheca, however, further examination provided enough evidence that the species were in different. So this species was identified as N.vreisii in the genus Nannizziopsis.[3]

CULTURAL CHARACTERSTICS:

This fungii in culture produces dense colonies of diameter ranging from 25-30 mm within 14dys .The culture appears white and powdery with the reverse side having a yellowish color.[4] Isolates are shown to have strong urease activity and are mesophilic with optimum growth observed at 30°C. The growth of N. Vriesii is inhibited at temperatures below 20°C to 30°.[4] Unlike some closely related fungi, N.vriesii doesn't require an exogenous source of the vitamins thiamine or inositol for growth.[5]

PATHOGENESIS FOUND IN REPTILES:

Several researches have proven that the Chrysosporium anamorph of Nannizziopsis vriesis(**CANV)** causes dermatitis and cellulitis inreptiles for example; CANV was isolated from the skin of chameoleon[5] , geckos[6]and more recently coastal bearded dragons whichhad nodular lesions and crusty debris on the skin[7] .They also been associated with poor nutrition which makes reptiles more prone to infections as a whole. Once the skin becomes infected,there is an accelerated risk of creating deadly circumstances which is called as Yellow fungus. However,N. vriesii are contagious and often fatal if not properly treated.[7]

SYSTEMATIC FUNGAL DISEASES IN HUMANS :

The impact of fungi on human health has been underappreciated, despite the fact that these eukaryotic pathogens infect billions of people worldwide, killingin excess of 1.5 million per year.

It was seen very rare in humans until the 1950s, with the revolution of contemporary remedy i.e antibiotics; development of intensive care units; the begin of the use of immunosuppressive agents (eg corticosteroids); the development of cancer chemotherapies, the inception of catheters where the fungi able to exploit humans in new ways. Fungal infections are determined by the fungal species and the immune status of the person infected. These invasive fungal diseases impose a major public health burden, with mortality rates of 30% to 90% , depending on the pathogen and patient population.

Superficial infections are the most common and include the 1 billion people with skin, hair, and nail infections. Mucosal infections with Candida (so-called "yeast infection) are alsoare chronic very common eg over 135 million women afflicted repetitively. More devastating are chronic, localized infections below the skin that are more common in tropical regions, as with mycetoma and chromoblastomycosis, which the World Health Organization (WHO) has recently classified as Neglected Tropical Diseases. Chronical fungal lung infections are complications of tuberculosis and other chronic pulmonary diseases, affecting millions globally. Fungal allergy common, with millions affected, worseningasthma and cystic fibrosis or leading to chronical nasal and sinus symptoms. Invasive fungal infections are progressive and lethal if not diagnosed and specifically treated.[8]

PONTENTIAL CAUSES OF YELLOW FUNGUS ON HUMAN RISK:

Depending on your health and risk factors, yellow fungus infections can strike as a primary or secondary infection. However from what has been evidently seen so far, the risks continue to be aggravated for those people who have compromised immunity, frail health or suffering from pre- existing problems like uncontrolled diabetes, high cholesterol, which cause inflammation and reduce the body's ability to fight off infections.

As seen with COVID- recovered cases (or those in the middle of recovery), a rise in fungal infections has been prescribed steroid use. The usage of steroids have now come under scrutiny from leading medical authorities. It can

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also develop on the skin after the fungus enter the skin through a cut, scrape, burn, or other type of skin trauma. Additionally, theCenters of Disease Control and Prevention (CDC) state that the risk of fungal infections are also high for the people who have spent a long time under intensive care units (ICU) and had an organ transplant recently, suffering from immune complications or low WBCs counts, who are dependent on extensive antibacterial or steroid use.

The need of hour is to maintain the required level of hygiene during treatment. As are we are living amid a pandemic and the rush in hospital in very high.

Symptoms in COVID Patients:

Signs and symptoms of Mucormycosis depend on the location in the body of the infection. Infection usually begins in the mouth or nose and the enters the central nervous system via the eyes.[9]

If the fungal infection begins in the nose and extends to brain, symptoms and signs may include one sided eye pain or headache, and may be accompanied by pain in the face, numbness, fever, loss of smell, a blocked nose or runny nose. The person may appear to have sinusitis[11]. The face may look swollen on one side, with rapidly progressing "black lesions" across the nose or upper inside of mouth. One eye may look swollen and bulging, and vision may be blurred[9, 11, 12].

Fever, cough, chest pain, and difficulty breathing, or coughing up blood, can occur when the lungs are involved. A stomach ache, nausea, vomiting, and bleeding can occur hen the gastrointestinal tract is involved[13]. Affected skin may appear as a dusky reddish tender patch with a darkening centre due to tissue death. There may be an ulcer and it can be very painful[10].

Invasion into the blood vessels can result in thrombosis and subsequent death of surrounding tissue due to a loss of blood supply[10]. Wide spread mucormycosis typically occurs in people who are already sick from other medical conditions, so it can be difficult to know which symptoms are related to mucormycosis people with disseminated infection in the brain can develop mental status changes or coma[10,14].

DISSCUSSION:

Nannizziopsis species belongs to the Onygenaceae family which includes the dermatophytes. They are keratinophilic microfungi, the ecology of which is not well known.

Fungi previously referred to as the Chrysosporium anamorph of Nannizziopsis vriesii are known to cause dermatological lesions of reptiles, both in captivity and in the wild[9]. Multiple cases of infection caused by these fungi have been reported with aggressive, pyogranulomatous lesions that can effect the skin, integument and musculoskeletal systems of snakes, chameleons, geckos, lizards and crocodiles [10, 11, 12, 13, 14, 15]. These reports are mostly from USA and Canada, but also Australia [12], Belgium[16] , Spain [14], Scotland[17] and Russia [15], and from most of the reports the infections often prove fatal in reptiles and appear to be highly transmissible between animals kept in confinement together, but do not infect humans. The clinical course tends to be of a rapidly progressing, deep, necrotic or granulomatous dermatomycosis that eventually disseminates and for which the outcome is usually fatal [18]. There are however reports of reptile infections being successfully treated with Itraconazole or voriconazole [16].

Case reports of Nannizziopsis species infections in humans are rare and, as far as the authors are aware, there are no reports of disseminated infection with N. obscura, as was seen in this patient, although there have been isolated reports from America of disseminated infection in both immune competent and immunocompromised patients with N. hominis [18].

Sigler et al. at the University of Albert microfungus laboratory studied six Nannizziopsis isolates from human samples (together with over forty isolates from reptiles) and from these isolates confidently identified three distinct species that have been found in humans; N. hominis, N. infrequenes and N. obscura [18]. N.infrequenes was found in the bronchial lavage sample of HIV positive 40 year old male patient being treated for pneumonia in Atlanta in 2004

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with a CD4 count of 13. However, it was not thought to be pathogenic and the patient recovered without being treated with antifungals [19].

N. hominis was isolated in 1994 from a deep muscle mass on the right thigh, right groin, buttock and lung of an HIV positive male in California who died eight months after the initial isolation. The patient received itraconazole for the fungal infection. The isolate from the lungs had been tentatively identified initially as a Trichophyton species[18].

In 2000, a white mould was isolated from the swollen lymph nodes of an immunocompetent Nigerian man from Boston who presented with disseminated adenopathy following a trip to Nigeria. One of the isolates from this patient tested positive in the AccuProbe Blastomyces culture identification test and was referred on to a laboratory in Texas for further evaluation. Because of its Chrysosporium - like morphology, the isolate was then forwarded to specialists at the University of Alberta microfungus laboratory for further review. The patient was readmitted to the hospital six months later and found to have a disseminated fungal infection involving the heart (endocarditis), lungs, spleen, and kidneys. The fungus was not grown again, but the patient had been on itraconazole since the initial diagnosis and remained on the drug for two years. The original isolate in this case was thought to be N. hominis[18].There has been one confirmed reported case of N. obscura infection in humans before and Sigler et al. identified one further possible case of N. obscura infection in their analysis too [18].

In 1984 a black African 24 year old male patient presented to orthopaedic surgeons in New York with swelling of his right ankle. X-rays showed a large lucency in the distal tibia and tissue samples were positive for what was identified at the time as a Chrysosporium species. The patient was not known to be immune compromised but had travelled to Africa in 1975, at which time he had been involved in renovating a house, being exposed to lots of dust. He denied any pulmonary symptoms and apparently recovered following a four month course of amphotericin B[21]. Sigler et al. identified this isolate as N. obscura in their analysis in 2013 [18].

An isolate causing a brain infection in an HIV positive Nigerian male in Germany was identified as Chrysosporium anamorph of Nannizziopsis vriesii, but no details on the methods used to identify the fungus were provided [22]. This was a 38 year old man who presented to neurosurgeons in Hamburg in 2005 with an eight month history of parietal headaches, poor memory, left arm paraesthesiae and left sided focal seizures. His viral load was undetectable on antiretroviral treatment and he had a CD4 count of 102. MRI brain showed two large abscesses in the right hemisphere with associated odema. The pus drained from these abscesses grew what was initially identified as N. vriesii and he apparently responded to treatment with voriconazole, steroids and anticonvulsant medication[22].

CONCLUSION:

As the fungal infections have taken faster growth in COVID patients and causing risk to humans. Where these observations show how difficult this infection is to detect, which could explain why so few cases of human infections have been reported. However, the diagnosis of these cases since 2015 suggests that the prevalence of Nannizziopsis infections may be underestimated.Since the damage caused by the infection is said to be much more dangerous and severe, experts now warn people to start recognizing the infection from day 01 and seek help.It should treat with antifungal drugs in earlier when detected. People should be aware of fungal infections and should maintain hygienic living.

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