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Disseminated Blastomycosis in a local farmer from Himachal Pradesh, North India: A diagnostic dilemma

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Abstract:*Blastomycesdermatitidis has been isolated only infrequently from environmental sources and thus the ecology of B. dermatitidis remains incompletely understood. Other methods of detection of prevalence are also insensitive. Our knowledge is based on the collected reports of sporadic cases in humans and dogs as well as the studies of 11 epidemics or clusters of disease. It can mimic many diseases and may remain undiagnosed till late. In disseminated infections, without treatment mortality remains high (78%). Most cases reported from India are imported from USA. We are reporting a case of Disseminated Blastomycosis acquired in North India in a native farmer. Its diagnosis remained a challenge in our laboratory setting.*
Keywords:*Disseminated Blastomycosis, North India, DGI.*

I. Introduction

Blastomycosis is an uncommon, geographically restricted, systemic mycoses, caused by the thermally dimorphic fungus, *Blastomycesdermatitidis*.Its endemic areas in North America and Africa are along the river basins. In India, its areas of environmental distribution and prevalence remain undetermined and there are only few well documented cases though it is strongly suspected to be endemic.[1,2]Here, we are presenting a case of disseminated blastomycosis in a native farmer from Himachal Pradesh, North India and challenges encountered in a routine microbiology lab in reaching the diagnosis.

II. Case Report

A 65 Year oldfarmer, a widower for 15 years, living in the surroundings of Satluj river in the Mandi district (H.P.) presented in the Dermatology OPD with :-
Painful joints with low grade fever, off & on – 3 months
Pustules over face &extremities – 5 days
Painful swelling of scrotum with pus discharge - 5days
Whitish discharge after micturition – 5 days

Clinically, Disseminated Gonococcal Infection (DGI) was suspected though there was no history of any sexual contact in past 15 years. Patient had never travelled abroad.On examination, there were papulopustular lesions on the exposed parts of body (figure 1) and the scrotum had typical "watercan perineum" appearance with multiple sinuses. Crepts were present over right lower part of chest. Abdomen and CVS had normal findings. Swabs from pustules, scrotal pus discharge and urine sample were submitted for microscopy and culture for gonococci. Gram stain and its modification with neutral red as counter stain were used to stain smears from all the samples. All samples were inoculated on Blood agar, Chocolate agar, MacConkeysagar and Mueller Hinton agar. They were incubated in a candle jar at 37^{o}C.

Smears were negative for gonococci. But all samples showed broad based budding yeast cells with double walls. These structures were initially overlooked by reporting residents as juniors kept looking onlyfor gonococci and seniors presumedit to be a stain contamination with yeast.After 48 hours of incubation, cultures showed white, creamy, smooth colonies on blood and chocolate agars. There was no corresponding growth on MacConkeys agar. Mueller Hinton agar was used to isolate gonococci but an off white, filamentous, spiky, confluent fungal growth was obtained after 4 days. It was sent to mycology lab for identification where it was accidentally discarded presumed to be fungal contamination.From scrotal pus discharge a mixed growth of *Proteus vulgaris* and *Enterobacter spp.* was isolated and sensitivity was reported.

On smears, broad based budding yeast cells (Figure 2) were picked up by a consultant and simultaneously culture isolates alsoshowed presence of yeast cells. Results were correlated and further isolates were processed on SDA and Blood BHI agar to demonstrate thermal dimorphism (Figure 3). At room temperature growth was dry, wrinkled and spiky again (left culture bottle in Figure 3) and showed transitional forms i.e. both filamentous and yeast forms (Figure 4). Growth was pure but spores and pure filamentous growth was not obtained despite several attempts. Growth was preserved in several vials of SDA. It was sent to

Department of Microbiology, PGIMER, Chandigarh, India (reference center)where it could not get recovered after 2 months of preservation and molecular identification could not be done.

Patient eventually developed features of CNS & eye involvement. Yeast cells were detected from CSF, soft palate lesion, nasal scraping and sputum. X-ray chest also showed infiltrations. HIV test was negative.Patient remained admitted for 3 weeks. He was given Amphotericin B intravenously. He developed side effects of high fever with shaking chills. His serum creatinine levels also rose significantly. Finally, he developed DIC and became LAMA.

III. Discussion

Blastomycesdermatitidis grows in geographically restricted microfoci in proximity to waterbodies associated with soil rich in organic matter, in shaded areas. Foggy weather helps in release of microconidia which are infective forms and inhaled by the host.[3]There is an association between cases of blastomycosis and the presence of scrub and mature pine habitat. This has led to a hypothesis that after a period of measurable precipitation, a dormant natural reservoir is maintained in the acid decay of conifers.[4]It is also associated with the presence of salamanders of the *Necturus genus*.[5] Our patient also belonged to similar climate and lived near river Satluj in Himachal Pradesh which too has a coniferous flora.

Epidemiological tools like use of skin test surveys, selective media for isolation from soil and serological studies available for other systemic mycoses are not effective against blastomycosis.[6] Recent application of PCR for rapid detection of *Blastomycesdermatitidis* in clinical and soil sample is highly promising.[1] Epidemiologic features, such as activity in a riparian area, outdoor recreation, brushwork, travel to hyperendemic areas, dog bite or recent death of a pet dog due to pulmonary disease has been found as exposure factors.[4] Veterinarians must be alert to this infection in canines in suspected areas.[5]

Systemic infection occurs by inhalation of mycelial fragments/conidia and localized cutaneous infection by direct inoculation of skin.[7]The incubation period is 4-8 weeks and 1-5 weeks, respectively.[3]Transmission of this infection through prostatic fluid, which is a unique characteristic among systemic mycosis, was documented in 1983. This characteristic can make this mycosis a potential sexually transmitted disease.[5]It is a systemic pyogranulomatous infection, primarily involving lungs. Disseminated involvement is common for skin, bones and genitourinary system, but almost any organ can be infected.Skin disease is the most common extrapulmonary manifestation and a marker for multiorgan infection.[6] Skin and mucosa involvement is often misdiagnosed as Squamous cell carcinoma. Pulmonary disease may be acute or chronic and mimics infection with pyogenic bacteria, tuberculosis, other fungal infections, sarcoidosis and malignancy.[6,8]Majority of cases are sporadic or endemic, epidemics associated with exposure to common outdoor source are documented.[7]Genito-urinary involvement is also seen in cryptococcosis and pneumocystis.[8] Disseminated gonococcal infections (DGI) occur mostly in women and are seen as hemorrhagic papules and pustules with purpuric centers in a centrifugal distribution. There is lower incidence of DGI at present in comparison to 1970s attributable to a decline in the particular strains that are likely to disseminate (PorB.1A serotype, highly susceptible to penicillin & AHU auxotype).[9]

Microscopically, yeast cell with 8-14 µ in size, a single broad based bud, a thick wall and 2-4 nuclei is pathognomonic of blastomycosis.[3,5]The yeast cells when found without buds may be confused with the immature spherules of *C.immitis, C. neoformans* without capsule or an unbudded yeast cell of *P.brasiliensis* and yeast forms of *H. capsulatum var. duboisii*with microforms of *B. dermatitidis* (3-5µ).[3] Several staining methods and searching for more definitive forms can help but morphology is presumptive method of identification and the specific nucleic acid probe is confirmatory.[3,7]Culture isolation and thermal dimorphism are important for diagnosis. Many strains do not convert completely and show transitional forms.[3]They are slow growing (10-30 days) except in heavy infection (1 week).[8]*Blastomycesdermatitidis* belongs to level 3 of the Biological Hazard Classification, which corresponds to agents that can cause disease in man and represent a danger to workers with the risk of propagation and for which there is effective treatment and prophylaxis as a result. The handling of these cultures must always be done in a laminar flow hood.[5]Some molds like *Pseudollescheriaboydii* and *Chrysosporium sp.* have similar appearance but they do not grow on media containing cycloheximide and later does not grow at 37°C. Several means of verifying the identity of *Blastomycesdermatitidis* have been developed: exoantigen test, DNA probe, PCR, sequencing and DFA.[7] Antigen detection in urine/CSF/serum/BAL is promising though it cross reacts with histoplasmosis, it can be used to rule out these two infections.[8]The Infectious Diseases Society of America recommends that mild to moderatedisseminated blastomycosis be treated with itraconazole. Therapy begins with a loadingdose of 200 mg orally 3 times daily for 3 days, followed by 200 mg twice daily for 6-12months. Amphotericin B is recommended for severe disease. The lipid formulationsshould be administered at a dosage of 3-5mg/kg intravenously daily until clinicalimprovement is noted; amphotericin B deoxycholate, at 0.7-1 mg/kg intravenously daily.After that, patients should receive a 12-month consolidation regimen of oral itraconazole.[10]

IV. Conclusion

Our experience makes us conclude thatthough clinical opinion helps a microbiologist in investigating the sample properly but it should not narrow the vision and approach to the sample processing and its outcome. White molds should be processed carefully in a biosafety cabinet.They should not be ignored as contaminants. Preservation of cultures should be done appropriately to investigate them in future. A high index of clinical suspicion coupled with pro-active mycological investigation is likely to reveal the occurrence of many more autochthonous cases of Blastomycosis from India.

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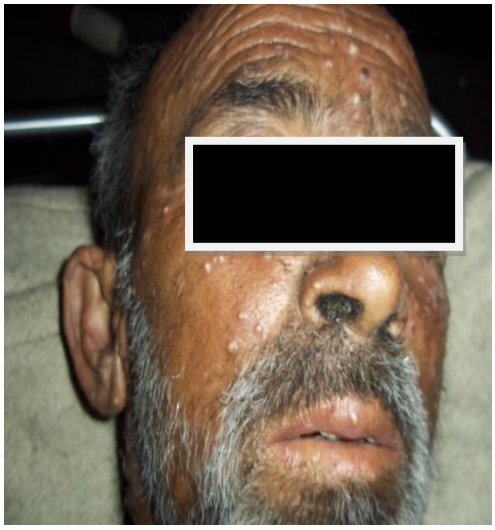

Figure 1 Disseminated papulo-pustular lesions over face.

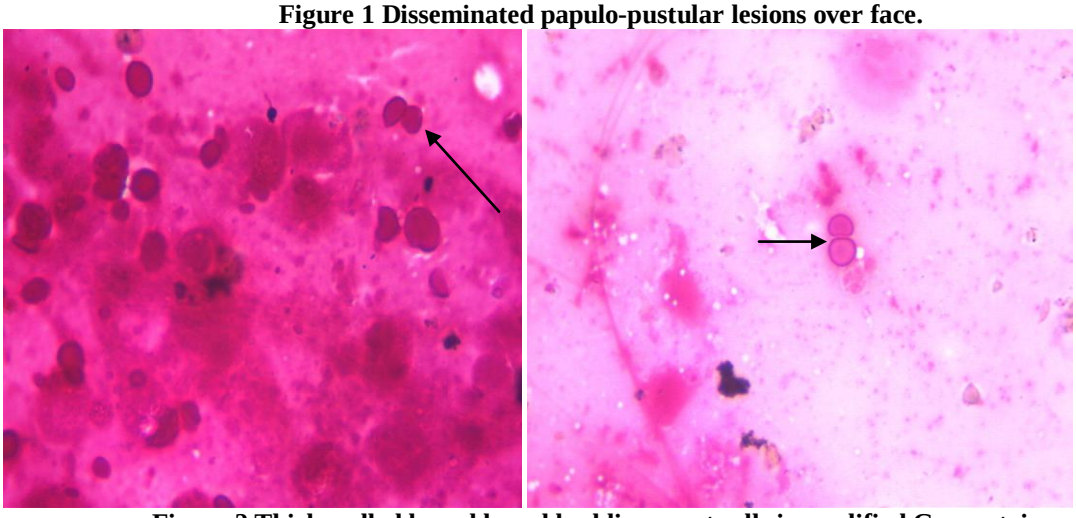

Figure 2 Thick walled broad based budding yeast cells in modified Gram stain.

Figure 3 Showing thermal dimorphism of growth.

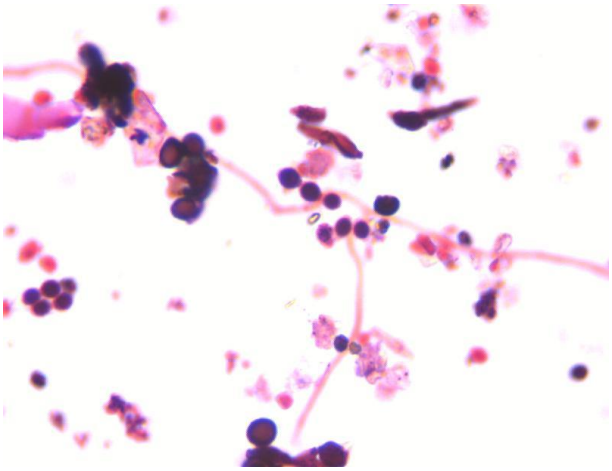

Figure 4 Transitional forms showing both hyphae and yeast cells on culture at 25°C