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(RESEARCH ARTICLE)

Blastomycosis: Report of a case from North India and its current status in the Indian subcontinent

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Abstract

Blastomycosis is a rarely known disease in India. This review traces the misdiagnosed cases of the disease reported as early as 1925 and later till 1997. Of the several authentic cases reported from India, only two have been authentically diagnosed autochthonous cases. Our case diagnosed on histological basis had a diagnostic dilemma as one of the PAS stained tissue section from the lesion showed slightly elongated yeast cells though these were with multiple budding. With the help of academic colleagues (joint authors in the paper), diagnosis of this case as blastomycosis was confirmed by latest molecular techniques as described in the case report. The clinical and diagnostic features of human autochthonous cases are reviewed. There is only known report of canine blastomycosis from India. It is suggested additional canine cases should be looked for in different parts of India to facilitate detection of endemic foci of *B. dermatitidis* in the country.

Keywords: Blastomycosis; Autochthonous cases; Indian subcontinent; North India

1. Introduction

Blastomycosis is a systemic mycosis caused by thermally dimorphic fungi, *Blastomyces dermatitidis* and *B. gilchristii*. Infection is acquired by inhalation of the organism, followed by its multiplication in the lungs, frequently disseminating hematogenously. Direct inoculation of the fungus is a rare means of infection [1]. The incubation period varies from 2 to 15 weeks, and the clinical spectrum ranges from asymptomatic to life-threatening infections involving acute respiratory distress syndrome or extrapulmonary dissemination [1]. Most identified cases involve pulmonary infection that manifests similarly to other causes of pneumonia [1,2,3]. The clinical similarities between blastomycosis and other pulmonary infections often result in diagnostic delays and unnecessary empiric antimicrobial drug treatment for suspected bacterial pneumonia [3]. The endemic areas for blastomycosis include states and provinces along the Great lakes, and Ohio, Mississippi, Missouri, and St. Lawrence river, Canada, Europe, Central America and India [1,4]. In a review of autochthonous cases of blastomycosis from reported from Africa and India [5]. It was found that 100 patients with this disease were reported from 12 African countries, whereas only 10 were described from India. Diagnosis of blastomycosis is usually confirmed by culture and phenotypic identification of the etiological agent; real-time PCR is also employed by some investigators [6]. Schwart et al 2018 [8] described a new species of Blastomyces, *Blastomyce helicus*, an emerging pulmonary and systemic pathogen for humans and animals in western Canada and United States. No case of *B. helicus* infection is known form Southeast Asia and including the Indian sub-continent.

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The earliest report of Blastomycosis from India was by Ganguli in 1925 [9], found to be a very common affliction, prevalent in the rainy season, generally affecting10 to 40% of the coolies working in the tea gardens of Duar situated between Cooch Bihar and Bhutan. From the lesions described as multiple warty ulcerated growths sometimes appearing granulomatous and the detection of round yeast like cells in scrapings of the lesions described by Ganguly [9], this report evidences a misdiagnosis of blastomycosis. In the same year Panja [10] also described a case of generalized blastomycosis with nodular skin lesions and yeast-like cells in skin scrapings; obviously it was again a case of misdiagnosis. Randhawa et al [11] have reviewed the 11 cases of blastomycosis reported in India including seven misdiagnosed, four authentic cases comprising two imported ones and two autochthonous cases including one from Uttar Pradesh and the other from Madhya Pradesh Subsequent to this review, there have been six reports of blastomycosis including two misdiagnosed cases from Gujarat [14, 15] and authentically diagnosed comprising one each from Haryana [16], Uttar Pradesh [17], Himachal Pradesh [18] and from Andhra Pradesh [19] two from Gujarat [20, 21], and one each from Arunachal Pradesh [22] Andhra Pradesh [23], Tamil Nadu [24] and Kerala [25]. Thus, the total number of authentic cases of blastomycosis reported so far from India is ten. Literature search also revealed from two authentic case of blastomycosis from other countries in the Indian subcontinent, one indigenous case in Bangladesh [26], and the other imported case in Nepal [27]. We report here a case of blastomycosis in migrant worker from Bihar in North India, diagnosed on histopathology and qPCR of paraffin-embedded tissue sections and give an update of the current status of blastomycosis in India.

2. Material and methods

An exhaustive search of the literature was made in PubMed, Medfacts, Medliine, Science Direct, National Centre for Biological Information (NCBI), Google Scholar, Research Gate, Mycology database.

3. Results

3.1. Case report

A 70-year-old male, an immigrant labourer from Bihar, presented with swelling of seven months on the dorsum of the foot, gradually increasing in size. The lesion was 5x2 cms in size and deep dermal. The overlying skin was unremarkable. He was HIV negative and was not able to recall any history of trauma. He was non-diabetic, non-hypertensive, and HIV negative, and did not have any cough or COPD. There was no family history of tuberculosis, or any other immunosuppressive disorder. He had no history of ATT and was a non-smoker and non-alcoholic. His blood profile was as follows: Hb 12gm/dl TLC- 9000/cumm DLC- P64 L31 M 2 ESR 25mm/1st hour Westergren. His blood sugar level was 90 mg/dl and kidney, and liver function tests were within normal limits. A solid-cystic mass (5x3 cms) was removed for histopathology. The patient was lost for follow-up and could not be traced for follow-up. Histopathological examination revealed central necrosis surrounded by histiocytes, lymphocytes and numerous multinucleate giant cells surrounding multiple broad-based multiple budding cells characteristic of Blastomyces, or Emergomyces. Surrounding dermis showed only mild lymphocytic inflammatory infiltrate. Overlying skin was unremarkable. Cultures of a portion of the biopsy were unsuccessful. The patient was lost for follow-up and could not be traced. The case presented a diagnostic dilemma as a couple of PAS-stained tissue sections showed elongated, encapsulated budding yeast cells, suggestive of *Histoplasma capsulatum* indicated by an arrow (Fig. 1).

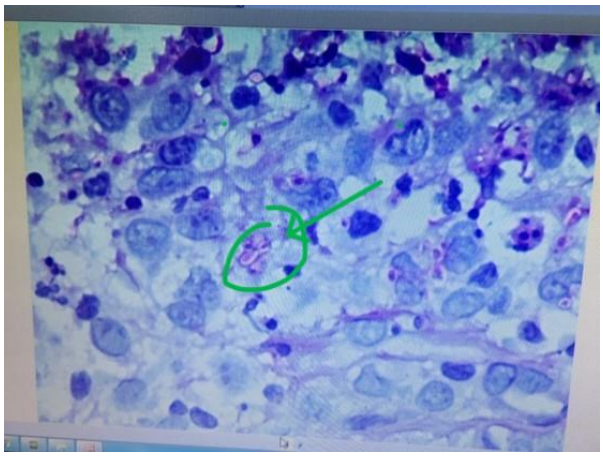

Figure 1 PAS stained tissue section

We sent the unstained paraffin embedded tissue sections of the lesion to Ricketts Volker, Germany. In his laboratory two broad-range PCR assays (targeting the ITS region) were conducted and amplicon identification performed by hybridization on chips. These chips could not identify DNA of *Histoplasma*, *Blastomyces dermatitidis*, *Paracoccidioides*, *Talaromyces marneffei* and *Coccidioides*. No hybridization was detected with controls demonstrating a correct hybridization procedure. Later Dr. Ilan Schwartz Department of Medicine, Faculty of Medicine and Dentistry, University of Alberta, Canada confirmed diagnosis of blastomycosis by qPCR assay with amplification of DNA on unstained paraffin sections and by demonstration of yeast cell characteristic of *Blastomyces dermatitidis* in tissue sections stained by GMS (Fig. 2).

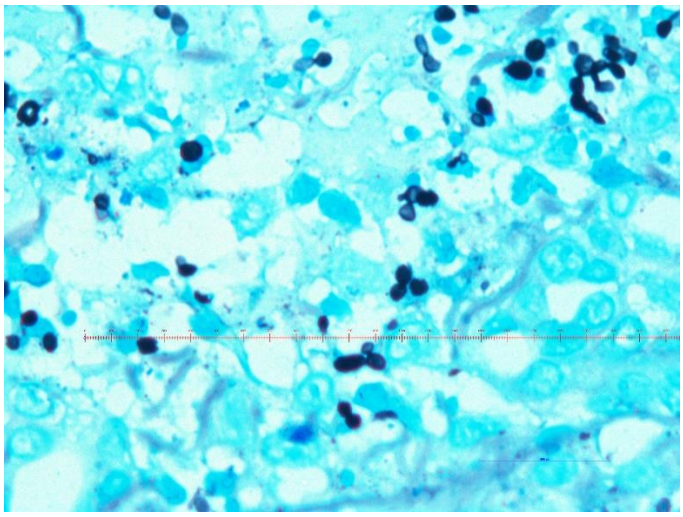

Figure 2 GMS stained image of suspected Emergomyces in tissue

4. Discussion

Randhawa et al in their review [11] mentioned two authentic cases of blastomycosis from India including one each from Uttar Pradesh [12] and Madhya Pradesh [13]. Our review has located seven more indigenous cases in India – one authentic each from Haryana [14], Uttar Pradesh [15], Himachal Pradesh [16], two misdiagnosed cases from Gujarat [17,18], and one authentic case each form Arunachal Pradesh [19], Andhra Pradesh [20], Tamil Nadu [21] and Kerala [22] and one each from Bangladesh [23] and Nepal [24]. Brief clinical and demographic feature of these cases and our own case from h are described in the table 1.

Though the total number of authentic indigenous cases known from India so far including the one from Bihar state being described here is only nine, but their locations are widely spread in several parts of India indicating that many more cases of blastomycosis possibly exist in country.

Pulmonary tuberculosis is very common in the Indian subcontinent and is often treated empirically. Mycological investigation cases of tuberculosis negative for culture and AFB smear and not responding to anti-tubercular therapy may reveal some cases of blastomycosis. The areas of environmental distribution of *B. dermatitidis* in India remain undetermined. Isolation of *B. dermatitidis* has been reported from the lungs of the bat, *Rhinopoma hardwickei hardwickei* [25] and the liver of the same bast species in India [26]. A mention may be made here of a report of pulmonary fatal blastomycosis in an Indian fruit bat (*Pteropus giganteus*) in USA [27]. It is not known whether bats could be a reservoir for human infections due to this fungus. In the USA, blastomycosis is very common in dogs residing in or visiting enzootic areas, and the incidence of blastomycosis in dogs is eight to ten times higher than that in humans [4]. Most dogs get infected by inhaling spores of *B. dermatitiids* from soil organic debris. Detection of blastomycosis in dogs is a sentinel of possible occurrence of human cases of this disease [4]. There is one reported case of canine blastomycosis from India in a Mongrel dog, found dead in 1982 in Bareily, Uttar Pradesh by Iyer [28]. Blastomycosis is primarily a canine disease and occurs in dogs nearly 10 times more than in humans than in dogs [4]. Thus, surveillance for more canine cases in other parts of India may facilitate detection of endemic foci of *B. dermatitidis* in the country. In USA. Blastomycosis has been reported in wild wolves from Minnesota, USA [29] but there is so far no report of this disease wolves in India. Thus, it can be emphasized that blastomycosis is an unrecognized endemic disease in India, and many more cases of this disease occur in humans, dogs, and possibly in other canines in several parts of the country but have not been detected.

Table 1 Cases of Blastomycosis from different states of India, and from Bangladesh and Nepal

Cases from India	Symptoms	Basis of diagnosis	Therapy	Outcome	Reference / Authenticity
Haryana 40/M	The man w as found dead besides a railway track near his village in Haryana, North India for post-mortem analysis. His relatives gave history that the deceased maintained poor health since many years and was a chronic smoker. His immune status was not known.	Histo-pathological examnation of both lungs showed focally hemorrhagic necrotizing pneumonia. The alveoli and interstitium were filled with yeast forms of B, dermatitidis was present both intracellularly and extracellulary	Not given, as the patient was dead.	Not applicable	Rana et al. 2015 [14] Authentic
Uttar Pradesh /12 M	The child from a rural area had multiple hyperkeratotic plaques of varying size all over his body, Clinical examination showed some ox multiple ulcers on the neck exuding pus.	Histopathology of biopsy of lesions showed suppurative granulomatous infiltrate and broad-based oval budding cells consistent with that of *B. derrmatiitis* staining positive with PAS	The patient was started on oral itraconazole 5mg/kg/day and IV cefoperazone and sulbactam His skin lesions improved but he became unconscious on 4th day and was then treated with Ampho tericin B	The patient succumbed to death ont 15th day of admission.	Shekhar et al. 2017. [15]
Himachal Pradesh 65/M	Disseminated pulmonary infection with CNS and eye involvement	Demonstration of yeast cells characteristic yeast cells in CSF, sputum, nasal scrapings and soft palate lesion,	Intravenous Amphotericin B. The patient developed side reactions of shaking chills and high fever	He developed disseminated intravascular coagulation and became left the hospital against medical advice	Sharma et al. [16] /Authentic
Gujarat 37/M	Multiple small maculopapular, firm nodules with sinuses on the middle third of the dorsal aspect of the knee, h/o renal transplant	Clusters of yeast like cells and presence of IgG serum antibodies to *B.* *dermatitidis*. Cultures not successful	Initial treatment with fluconazole failed, switched to Itraconazole 400 mg daily. duration not mentioned	The lesions healed	Patel et al. [17] Not acceptable, as examination of the histology image in the publications shows one singly budding

					yeast cells and a pseudohypa
Gujarat 35/M	Multiple small vegetative over the upper limbs, lower right leg, a few ulcers on right arm and crusted ulcers over the mammary area	Diagnosed merely on appearance of the clinical lesions.	The lesions started to heal. The patient was given cefaxine and advised to stop smoking and alcohol consumption.	Not mentioned	Hongal and Geije [18] Not acceptable, as clinical lesions are rather suggestive of chromoblasto-mycosis
Arunachal Pradesh 53/M	Bilateral adrenal enlargement with mild cyanosis, clubbing, fatty hepatomegaly, mild spelnomegaly, h/o smoking for 39 years and diabetes for for five yeas 39 yrs. and diabetes for 5 yrs.	Demonstration of broad-based yeast cells in PAS and GMS-stained sections of adrenal biopsy, and recovery of *B. dermatiitidis* in culture of pus obtained by a repeat biopsy	Itraconazole 200 mg twice daily for three months	Monthly follow-up showed remarkable improvement with resolution of the lesion after three months as seen in USG of the abdomen	Kumar et al. 2014 [19] Authentic
4/M Andhra Pradesh	The child from a rural area had a 6-month history of multiple, hyperkeratotic, suppurating plaques and nodules over the face, chest, back and upper and lower extremities, with a huge intraocular flesh-colored mass in the left eye. Prior to this he had cough with fever, followed by a plaque over the right cheek with cervical lymphadenopathy. Chest X-ray revealed patchy consolidation of the upper lobes of the right lung. FNAC of the cervical lymph nodes showed non-specific lymphadenitis, and ATT was given While on ATT, he started developing multiple cutaneous lesions, nasal stuffiness causing airway obstruction and a large mass in the left eye causing proptosis. On the day of presentation, the child′s general condition was good. But on ATT, he started developing multiple cutaneous	CSF revealed high protein (600 mg/dL) with normal cell count and no acid fast bacilli and fungal elements were isolated.	The patient was given injection of dexamethasone 2 cc i.v. three-times daily and amphotericin B initially 0.25 mg infusion for 2 days as a test dose followed by 0.5 mg. The dose was gradually increased to 1 mg over a period of 5 days.	The patient did not respond. His general condition gradually deteriorated and he succumbed to death.	Rao et al. 2013 [20] Authentic

	lesions on several parts of the body, nasal stuffiness causing airway obstruction and a large mass in the left eye causing proptosis.				
Tamil Nadu Age?	Middle aged man with low grade fever and chronic cough for the last two months and shortness of breath on exertion. He was a chronic smoker (25 packs years). He had visited Ohio state, USA in the recent years for 3 months. His chest X-ray demonstrated a homogenous opacity in the left in the left lung field. A CT scan of the chest showed a mass lesion in the left upper lobe. His chest X-ray suggested lung malignancy. Because of sudden haemoptysis, he underwent lobectomy of the upper left lobe	Histopathology revealed patchy pneumonitis with extensive suppurative granulomatous inflammation with spherical to oval doubly contoured yeast cells consistent with that of *B. dermatitidis*	Oral itraconazole (dose not mentioned) for six months	The patient was doing clinically well on follow up visits	Joshi et al. 2022 [21]
32/M Kerala, an imported case from USA	Multiple discharging sinuses on the anterior chest wall, h/o of travel to Chicago, USA and ATT for 12 months		Itraconazole 200 mg twice daily for 12 months	The chest wall sinuses closed, and the sinus lines disappeared	Kumar et al. [22] Authentic
Cases from Bangladesh					
40/M	Single, w ell demarcated oval plaque with a few crusts on the lower part of chest wall in a case from Dacca	Demonstration of characteristic yeast form in KOH preparation of biopsy	Itraconazole 200 mg daily for three months	Cured	Bhuiyan et al. 2015 [23] /Authentic
Cases from Nepal					
60/F An imported case (a Nepalese immigrant in USA)	Pulmonary infection, multi-lobular consolidation and foci of necrosis in the lung, followed by a necrotic ulcer on the dorsum of the tongue, h/o Coombs-positive autoimmune hemolytic anemia, and diabetes melitus. Case diagnosed in USA after 9 months of his stay in Nepal	Broad-based budding yeast cells in PAS and GMS- stained tissue sections of a transbronchial biopsy and recovery of *B. dermatitidis* from tongue ulcer, BAL fluid and bronchoscopic biopsy	Oral itraconazole for 12 months	Cured.	Gandhi et al. [24] Authentic

Foot notes: COPD-Chronic obstructive pulmonary disease; FNAC-Fine needle aspirate; CT-Computer tomography; ATT-Antituberculosis treatment; PAS-Periodic acid shiff; GMS-Grocott-Gomori silver methenamine; FNA-; Fine needle aspirate; TB-Tuberculosis; BAL-Bronchoalveolar lavage

5. Conclusion

This study mentions the number of authentic cases of blastomycosis reported from several partsof India and from other countries in Indian subcontinent, namely, Nepal and Bangladesh. A case of blastomycosis in a Mongrel dog in Uttal Pradesh, India is also described. The importance of surveillance of canine cases of blastomycosis is emphasized.

Compliance with ethical standards

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Disclosure of conflict of interest

We have no conflict of interest with any individual or organization.

Statement of ethical approval

This study did not involve any human's subjects or animals and hence Ethical approval is not required.

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