

## FOCUS ON CRYPTOCOCCOSIS<sup>§</sup> (A clinico - mycological case report)

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### Summary

A case report of disseminated cutaneous cryptococcosis with Hodgkin's disease is presented. No foci in the lungs, central nervous system, bones, gastro-intestinal tract, liver, kidneys or heart were detected. *C. neoformans* was cultured, identified by its capsule, growth at 37° C, ability to produce urease, specific nitrate and sugar assimilation and pathogenicity for the mouse. Histopathologically the organism was demonstrated in the tissue sections. Clinical subsidence was seen with amphotericin B. 0.5mg/kg. for 22 days.

The fact that present day use of steroids, immunosuppressives and anti-neoplastic agents are known to predispose to this infection is emphasised.

Busse and Buschke in 1895 described the first case of cryptococcosis. A year earlier Sanfelice had isolated the organism. In 1952 Lodder and Kreger-Van Rij established the name *Cryptococcus neoformans* (*C. neoformans*) and Shadomy in 1970 described the perfect form of the organism. *C. neoformans* infects man, domestic and wild animals. Bovine mastitis is known to spread the infection. The organism has been isolated from natural sources, pigeon excreta and air samples. Initial infection is often pulmonary. Cutaneous Crypto-

coccosis reflects either disseminated disease or primary infection and accounts for 10% of cases. With the common use of corticosteroids, immunosuppressives and antineoplastic agents, the disease is being recognised more frequently lending support to the thesis that infection is much more common than the disease.

### *Incidence*

Littman and Walter<sup>1</sup> in a survey between 1952-53 reported 788 deaths in the U.S.A. due to cryptococcosis. The disease is seen in adults, shows no racial predilection and has a male: female ratio of 2:1. In the Indian literature Balkrishna Rao<sup>2</sup> first reported a case of cryptococcal granuloma of the brain. Ramamurthi et al<sup>3</sup> reported a spinal granuloma, Khan et al<sup>4</sup> reported pulmonary cryptococcosis, Sinha et al<sup>5</sup> cerebral Cryptococcosis and Basu Mallik et al<sup>6</sup> meningeal involvement with lung lesions seen at biopsy. Anguli et al<sup>7</sup> reported systemic involvement of the lungs, myocardium and kidney while Koshi et al<sup>8</sup> reported bone involvement.

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Sandhu<sup>9</sup> isolated *C. neoformans* from the sputum of a patient suffering from bronchitis. Ahuja et al<sup>10</sup> demonstrated the infection on laparotomy from a mediastinal mass. This patient also had pulmonary involvement. Subramanian et al<sup>11</sup> isolated *C. neoformans* from a case of meningitis. Aikat et al<sup>12</sup> presented 4 cases with meningo encephalitis, one of which was a one year old child. Mittal et al<sup>14</sup> reported a case of cryptococcal meningitis and so also Roy<sup>15</sup>. Shome et al<sup>16</sup> reported 2 cases of pulmonary cryptococcosis. Ichchaporria et al<sup>17</sup> reported a case of cryptococcal meningitis, Mukthabat et al<sup>18</sup> reported 3 cases with cutaneous and 1 case with pulmonary and meningeal involvement. Krishnakutty et al<sup>19</sup> reported cryptococcal meningitis. The paucity of cutaneous lesions of cryptococcosis seen, diagnosed and treated, successfully prompted us to report this case.

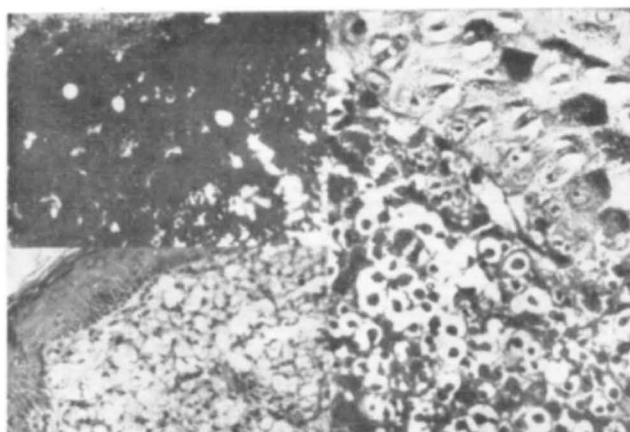


**Fig. 1** Cryptococcus infection (A) before and (B) after treatment

### Case Report

A 35 year old male patient, farmer by occupation was seen in the skin O.P.D. of Nair Hospital, Bombay. He complained of ulcers on the face and left leg for 2 months and acneiform lesions with ulceration on the face and shoulders for one month.

The patient was a known case of Hodgkin's disease with axillary and cervical lymphadenopathy; the diagnosis having been established through an axillary node biopsy. He was treated with 20 injections of endoxan when patient noticed the skin lesions and reported to us. On examination the lesions were found to be painless, well demarcated pinkish papules with no surrounding inflammation. They gradually enlarged with the centre softening and discharging a glairy, blood tinged pus to form a painless ulcer with slightly rolled and undermined edge and a floor with granulation tissue. (Photograph 1).



**Fig. 2** Upper left corner : Cryptococci demonstrated by India ink method  
Lower left corner : Section of the skin on H & E : taining showing masses of cryptococci resembling foam cells  
Right half : Section of the skin on PAS staining : Cryptococci in the dermis

### Investigations

Smear from the pus discharge on staining with India Ink showed the typical encapsulated yeast forms, the mucoid capsules appearing as transparent halos of variable thickness external to the cell wall. (Photograph 2).

The discharge was cultured on brain heart infusion agar and Sabouraud's dextrose agar (at pH 7.0) at 37°C. The typical mucilaginous colonies showed yeast like budding cells-pinched off; no mycelia and presence of capsules. The ability to produce urease and the specific nitrate and sugar assimilation confirmed the diagnosis of *C. neoformans*. Intracerebral injection in a mouse further proved the pathogenicity for mouse.

Skin biopsy - The PAS and H & E staining showed cystic areas containing masses of cryptococci (Photograph 11 B & C). The cryptococci appeared abundantly cystoid clusters centrally with a sparse peripheral inflammatory response. The Masson's alcian blue, Lillie allochrome and particularly the mucicarmine stains, showed distinctly the encapsulated *C. neoformans*. Culture of the sputum, urine, blood and C.S.F. were unrewarding. E.S.R. was 50 mm, of Hg. Gland biopsy showed features of Hodgkin's disease. X-rays of chest and skull were normal. Barium meal was normal. C. S. F. was normal. Liver function tests and E.C.G. were normal.

### Treatment

The patient was given initially I.V. 0.25 mg/kg. of amphotericin B for 2 days and subsequently 0.5 mgs./kg. for 20 days. There was complete resolution of the skin lesions at the end of treatment.

### Discussion

The present day use of corticosteroids, immunosuppressives and antineoplastic agents has caused a rise to the incidence

of cryptococcal infection. This makes it mandatory for dermatologists to keep in mind the possibility of such when faced with unusual skin lesions in susceptible patient group. Further malignant disease of the reticulo - endothelial system itself is often associated with cryptococcosis. Approximately 30% of patients with disseminated cryptococcosis have been shown to have such a malignancy<sup>20</sup>. In our case the disease as well as the treatment with endoxan may both have contributed to the immunosuppression which in turn predisposed the patient to disseminated cryptococcosis.

This case fulfills all the criteria for the diagnosis of cryptococcosis in that on culture, the mucilaginous yeast like colonies were seen, with presence of a capsule, the ability to grow at 37°C, to produce urease and the specific patterns of nitrate and sugar assimilation along with the pathogenicity for the mouse. Histopathologically the skin tissue showed cystoid clusters centrally with abundant cryptococci and peripherally a sparse inflammatory response. The inert polysaccharide material of the capsule of cryptococci is responsible for inhibiting tissue response to antigens of the cell bodies and hence the sparse inflammatory peripheral response. The response to amphotericin-B was excellent.

### Conclusion

1. A case of disseminated, cutaneous cryptococcosis with Hodgkin's disease is presented.
2. Use of steroids, immunosuppressives and antineoplastic agents is known to produce the disease more frequently.
3. No focus in the lungs, C. N. S., bone, G. I. tract, liver, kidneys or heart was detected.
4. *C. neoformans* was cultured, identified by its capsule, growth at 37° C., ability to produce urease,

specific nitrate, sugar assimilation and pathogenicity for the mouse.

5. Histopathologically the organism was demonstrated in the tissue sections.
6. Clinical subsidence with Amphoterin B. 0.5 mg/kg. for 22 days.

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