

DISSEMINATED CRYPTOCOCCOSIS

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Infection with *C. neoformans*, a yeast-like fungus is being recognised more frequently than hitherto. The clinical diagnosis of Cryptococcosis is difficult. Symptoms of meningo-encephalitis are the commonest presenting feature of disseminated Cryptococcosis due to the predilection of the fungus for the C.S.F. (Moss 1960). The disease is frequently diagnosed by the discovery of the organism in the C.S.F.

Although neurological symptoms are common their presentation may be bizarre. The signs may be of meningeal irritation, a space occupying lesion, encephalitis, hemiplegia or coma, (Aberfeld and Gladstone 1967).

The case presented below is interesting as a clinico-pathological correlation. The wide spread systemic dissemination of the organism in relation to the paucity of presenting signs and symptoms is alarming.

CASE REPORT

The patient, S.N., African female, 45 years old, was admitted to hospital complaining of severe headache, dizziness and vomiting. The onset and duration of these symptoms were not ascertained. There was a past history of inguinal and axillary abscess: whether in addition to traditional medication, the patient received medical treatment for this is doubtful.

Physical examination was surprisingly unhelpful. The patient was afebrile. There were chronic puckered scars in both inguinal regions, both axillae and in the anterior cervical region. Moderate pitting oedema of both ankles was noted. The remainder of the systemic examination was negative.

The patient died about 30 hours after admission.

NECROPSY EXAMINATION

The significant necropsy findings only are presented. Moderately severe degree of emaciation. Puckered widespread scarring in both inguinal regions, both axillae and of the anterior cervical area with underlying matted enlarged caseous lymph nodes.

Respiratory System: There were bilateral sero-fibrinous effusions of moderate quantity and dense bilateral fibrinous and fibrous pleural adhesions. Both lungs were completely consolidated with active cavitating and caseating tuberculosis of the left upper lobe. The remaining left lung and the entire right lung showed pneumonic consolidation with a rather mucoid appearance suggesting Friedlander's pneumonia. The hilar glands were enlarged and caseous.

Gastro-intestinal System: The liver was moderately enlarged (weight 1650 g.) and had a nutmeg appearance. The spleen was enlarged (weight 350 g.), soft and diff-

luent. Miliary tubercles were not noted. Mesenteric lymph nodes were enlarged and caseous.

Genito-urinary System: The kidneys weighed 105 g. each, were relatively pale with cortical streaking. The para-aortic lymph nodes were enlarged and caseous.

Brain: Meninges were congested and thickened with patchy gelatinous exudate in the subarachnoid space at the base suggestive of Tuberculosis meningitis.

HISTOPATHOLOGY

Lung: Fibrocasseous tuberculosis of the left apex was confirmed. Sections from areas of pneumonic consolidation showed wide dissemination of yeast-like organism having the staining properties and microscopic characteristics of *C. neoformans*. The organisms were in the alveolar spaces (Fig 1). The apparent increase in

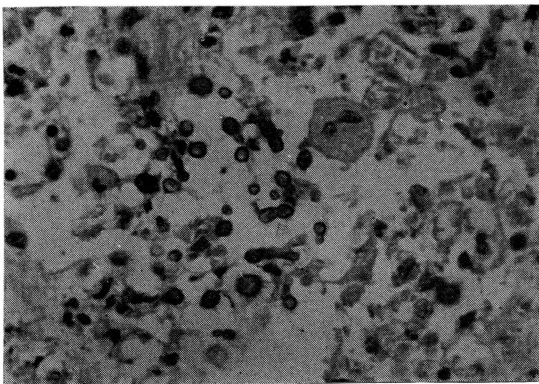


Fig. 1.

Cryptococcus neoformans in the lung. Budding forms are demonstrated and the amorphous exudate apparent. Foam cells are prominent while inflammatory cells are scanty. The mucinous capsule of the organism is clearly demonstrated. Mucicarmine X 360.

cellularity was not due to inflammatory exudate but rather to hyperplasia of the septal cells. Propagation by budding and the absence of hyphae, characteristic of Cryptococcosis, are well demonstrated in Fig. 1.

Brain: The subarachnoid space at the base of the brain was filled by an almost pure growth of Cryptococcosis (Fig. 2) with almost complete absence of inflammatory response. Only occasional macrophages and monocytic type of cells were noted. The organisms were also present in the perivascular space deep within the brain.

Liver: "Pseudo-microabscess" were prominent. There were microscopic lytic lesions in the liver parenchyma with colonies of Cryptococcus (Fig. 3) and surrounding monocytic cells. Plasma cells, neutrophils and lymphocytes were absent. It was these pale areas which gave the liver the macroscopic appearance of a nutmeg pattern.

Similar lesions were also noted in the glomeruli of the kidneys (Fig. 4), in the spleen and lymph nodes.

The striking feature in all sections was the almost complete absence of inflammatory exudate.

DISCUSSION:

C. neoformans (*Torula histolytica*) is a true yeast (Cruickshank 1967). It reproduces by budding without formation of mycelia. The organism is a saprophyte with world wide distribution. Cryptococcosis or torulosis is still, however, a relatively rare mycotic infection in man.

The clinical presentation of Cryptococcosis is often as an afebrile chronic meningitis. (Nichols and Martin, 1955, Moss and McQuown, 1960; Aberfeld and Gladstone 1967.) It may masquerade with bizarre presentations (Nichols and Martin; Moss and McQuown; Huang et.al, 1964; Symmers, 1953; Russel and Dean, 1957). It has a predilection for the central nervous system as the C.S.F. is an ideal culture media for cryptococcus. Before the advent of Amphoterecin B., cryptococcal meningitis was always fatal (Nichols and Martin; Moss and McQuown; Symmers; Russel and Dean; Huang et.al.; Vanbreuseqhem, 1958). Since the advent of Amphoterecin B., a recovery rate of nearly 80% has been achieved (Utz, 1967.)

Of the bizarre signs and symptomatology, violent, persistent headache associated with vomiting, is the most constant (Huang et. al.; Vanbreuseqhem; Nichols and Martin). In the case reported here the out-standing complaint was severe headache and this was associated with vomiting.

Many authors have noted the association of systemic cryptococcosis with other disease of the lymphoreticular system, the commonest being Hodgkins disease, lymphosarcoma and even with sarcoid. Vanbreuseqhem; Moss; Nichols and Martin). Consequently it has been postulated that systemic infection with cryptococcus is due to lowered resistance by the concomitant disease of the lympho-reticular system. It is interesting in this case that there was widespread involvement of the lymphatic system by fibro-caseous tuberculosis. It is probable that in wide spread disease of the lymphoreticular system there is suppression of the immune response thus promoting invasion by mycoses.

It is also known that *C. neoformans* is itself a very poor antigen (Utz). This finding is consistent with the histological appearances of cryptococcal lesions. All authors have stressed the feeble inflammatory reaction even in the presence of large numbers of organisms. This as stressed earlier was a prominent feature in this present case.

Unfortunately, in view of the widespread tuberculous involvement mycosis was not suspected at necropsy and tissue was not collected for culture. As Koch's postulate has not been satisfied, the diagnosis of *C. neoformans* in this case is presumptive. Nevertheless the organisms, as will be seen from the illustrations, were numerous and had the morphological characteristics of *C. neoformans*, and satisfied many of the requirements as listed by Symmers (1953) and MacGillivray (1966) for purposes of identification of cryptococcus in histology sections.

In view of the widespread use of wide-spectrum antibiotics and corticosteroids, systemic mycotic in-



Fig. 2.
Low power View of the brain showing an almost pure growth of *C. neoformans* in the sub-arachnoid space. Mucicarmine X 32.

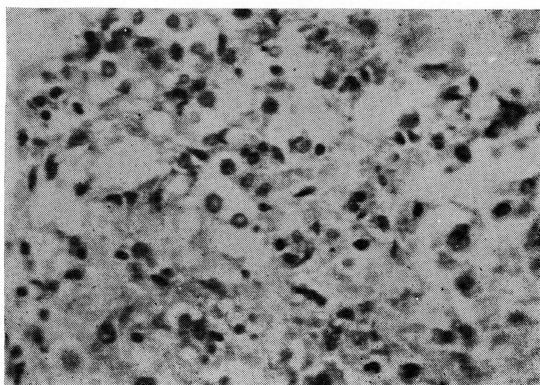


Fig. 3.
C. neoformans in liver. Liver cells show gross cloudy and fatty degeneration. These pale areas with surrounding normal liver parenchyma gave the naked-eye appearance of nutmeg liver. Mucicarmine X 360

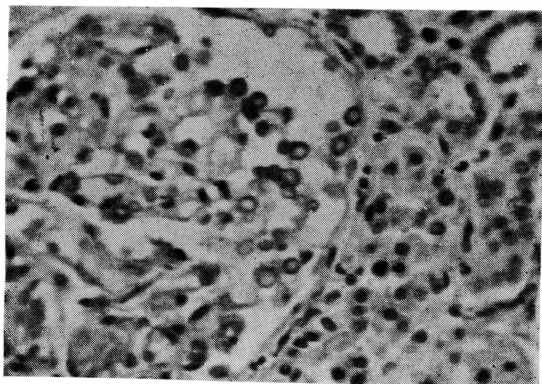


Fig. 4.
Large numbers of organisms in a glomerulus. The characteristic appearance of the organisms is again apparent. The total lack of inflammatory reaction is evident. Mucicarmine X 360.

fections are becoming more prevalent. For early diagnosis and successful management, fungal infections should always be considered in atypical presentations, in cachexia of malignant disease and in association with diabetes.

SUMMARY

A case of disseminated Cryptococcosis with concomitant widespread tuberculosis is described. Death was due to Cryptococcal meningo-encephalitis and Cryptococcal pneumonia. This, to my knowledge is the first case reported from this country but should by no means be accepted as the only case. I feel many cases are unrecognised.

ACKNOWLEDGEMENTS

I wish to thank Dr. J. C. Davidson for permission to publish the clinical details and to Dr. M. M. Nalumango, Permanent Secretary for Health, for permission to publish.

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