

PULMONARY AND MENINGEAL CRYPTOCOCCOSIS COMPLICATED WITH LUNG SCHISTOSOMIASIS

A Case Report

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S U M M A R Y

The Authors deal with a case of pulmonary cryptococcosis clinically manifested as a solitary moderately dense area of infiltration in the lung parenchyma (toruloma), which was treated by surgical extirpation. Cryptococci were largely demonstrated in the nodular pulmonary lesion. Pathologic changes in the surgical specimen were complicated by the coexistence of eggs and adult worms of *Schistosoma mansoni*. Focal pulmonary arteritis, focal pneumonic consolidation around *Schistosoma mansoni* eggs were largely seen in the pulmonary tissue outside the cryptococcal lesion. The patient developed a meningoencephalitic complication, the cryptococci being largely demonstrated in the spinal fluid. The patient was treated by intra-venous and intra-theal administration of Amphotericin B with relative improvement.

I N T R O D U C T I O N

Cryptococcosis (Torulosis) is a subacute or chronic infection caused by *Cryptococcus neoformans* (*Torula histolytica*), a yeast-like, non-sporulating, non-mycelial budding fungus exhibiting a marked tendency for the involvement of the central nervous system and lungs^{4, 17, 24, 26, 30} but not rarely producing lesions in the bones, skin, liver, kidney, as a result of a lymphatic or hematogenous spread²⁷.

Occasionally, the disease may be initially limited to the lungs^{1, 2, 8, 15, 20}. It has been postulated that the cryptococcal central nervous system involvement has resulted from dissemination of an initial pulmonary focus^{22, 27} although cryptococcal meningitis without

pulmonary involvement has been reported in the literature³⁴.

Cryptococcosis has been observed complicating pre-existing malignant diseases, chiefly malignant lymphomas and leukemias^{8, 18, 35}. In other cases the tissue response may resemble the non-caseating tubercles observed in sarcoidosis^{14, 27}. The association of cryptococcosis with parasitic diseases such as schistosomiasis⁵ seems to be a very uncommon finding.

In the present paper we deal with such an association occurring in a 40-year-old man who developed a solitary cryptococcal pulmonary lesion (toruloma) and who was treated by pulmonary lobectomy. Eggs as

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well as adult worms of *Schistosoma mansoni* were also found in the surgical specimen which gave rise to focal areas of pulmonary arteritis as well as focal pneumonic consolidation areas around the parasite eggs.

CASE REPORT

This 40-year-old mulatto man was admitted to the hospital presenting a flu-like syndrome consisting of low-grade fever, general malaise, weakness, cephalaea and cough with production of an abundant mucoid sputum. A chest X-rays taken on his admission disclosed a rather irregular solid density located at the superior third of the right lung (Fig. 1). Sputum examination stained by the Papanicolaou's stain showed great number of cryptococci which were better demonstrated after emulsifying the sputum with India ink

(Fig. 2). Sputum cultures on Sabouraud-dextrose-agar yielded the formation of creamy colonies on the fourth day of incubation at 20°C. Microscopic examination disclosed oval budding yeast cells. Laboratory studies showed a normal complete blood count.

The patient underwent right thoracotomy. The upper lobe contained a rather well circumscribed mass. There were no enlarged lymph nodes in the hilum. An upper lobectomy was performed. The gross examination of the surgical specimen showed a solitary encapsulated mass measuring 5.8 × 5.0 cm (Fig. 3) and exhibiting a characteristic mucoid slimy appearance on the cut surface.

Histologic examination showed numerous fungal cells filling and distending the pulmonary alveoli (Fig. 4). Groups of histiocytes were also seen within the alveoli. Occasionally, a tubercle-like reaction was seen around

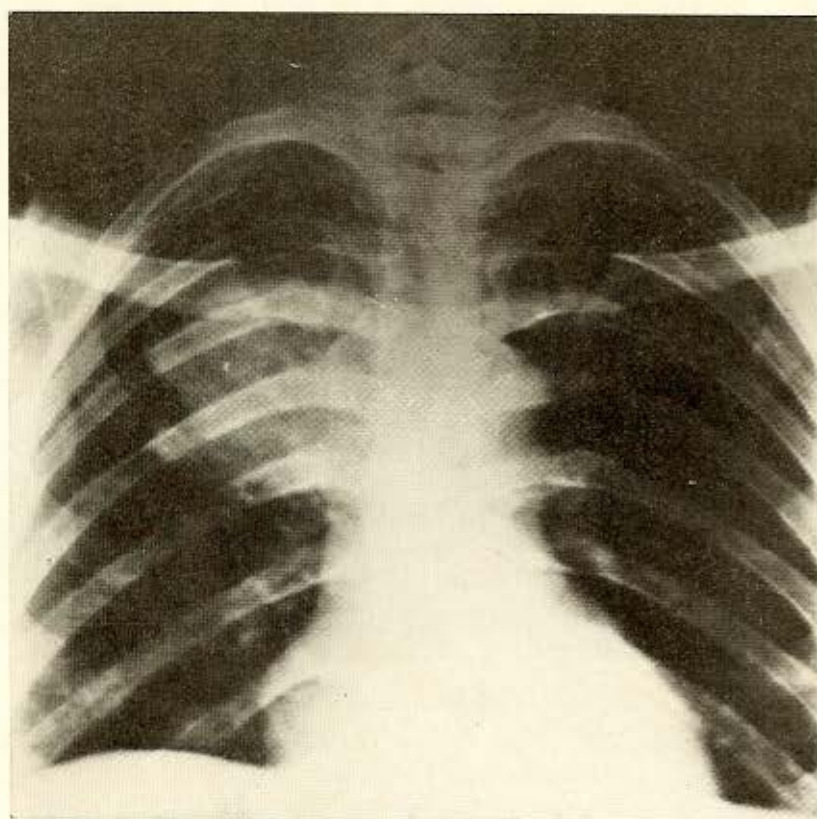


Fig. 1 — Chest film disclosing an irregular solid density in the right lung

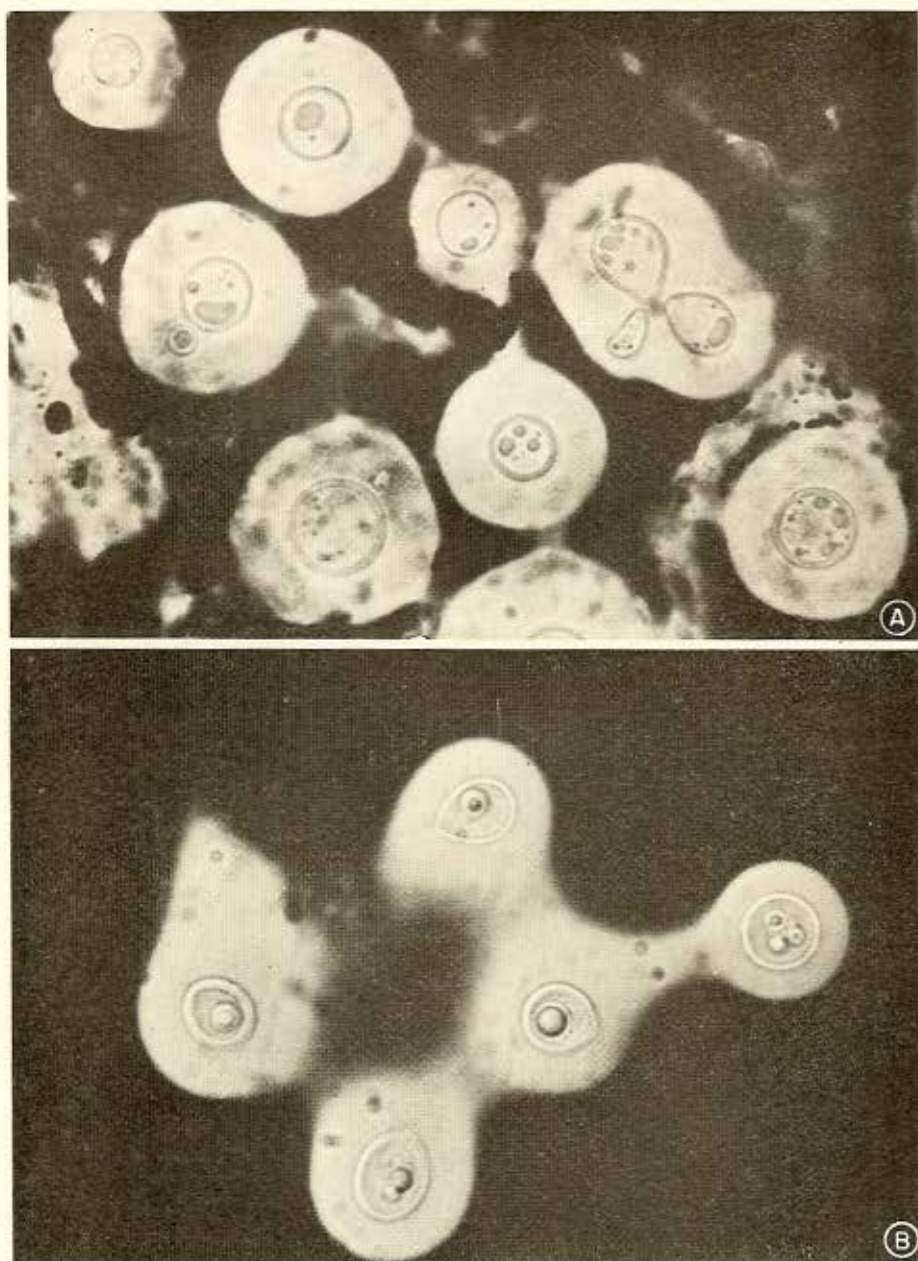


Fig. 2A) — India ink mount of sputum sediment containing budding *C. neoformans*. Note mucinous capsule appearing as a transparent halo. Hematoxylin Eosin. 1600 \times .
Fig. 7B) — India ink mount of spinal fluid sediment showing group of *C. neoformans*. Hematoxylin Eosin. 1600 \times

the yeast cells. In some areas the organisms were found within epithelioid multinucleated giant cells.

Outside the cryptococcal lesion there were many *Schistosoma mansoni* eggs located either extra-vascularly or impacted within the lumen of small pulmonary arteries and arterioles where they were seen causing a characteristic necrotizing vasculitis with destruction of the media and intima of the vessels. Many eggs were also seen surrounded by a dense fibrous collagenous reaction (Fig. 5). Occasionally, dense areas of pneumonic condensation were formed around *S. mansoni* ova. Adult worms were very often seen within dilated pulmonary vessels (Fig. 6). The patient had an uneventful postoperative course. However, four months after surgery, he complained of a marked cephalgia and tenderness of the neck. Physical examination showed nuchal rigidity with Kernig's and

Brudzinski's positive signs, besides marked papilledema. Spinal fluid emulsified in India ink showed numerous budding organisms surrounded by clear capsules (Fig. 7).

The patient was given Amphotericin B by intravenous and intra-thecal route with relative improvement. The meningoencephalitic picture disappeared and repeated spinal fluid examination failed to show more organisms, two months after the beginning of the treatment. Follow-up examination of the patient 6 months after chemotherapy revealed no evidence of meningeal involvement. Neurologic examination at that time disclosed primary optic nerve atrophy, ophthalmoplegia and deafness.

DISCUSSION

The lungs are among the most important and frequent anatomic site of cryptococcal

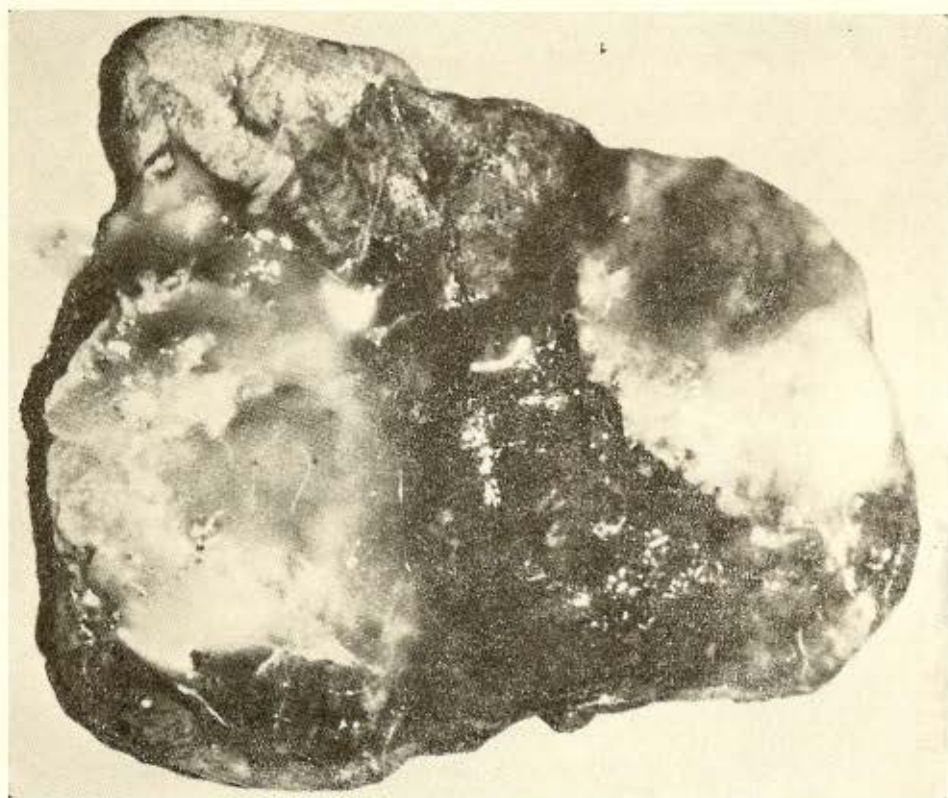


Fig. 3 — Surgical specimen showing great rather well delimited nodular mass (toruloma)

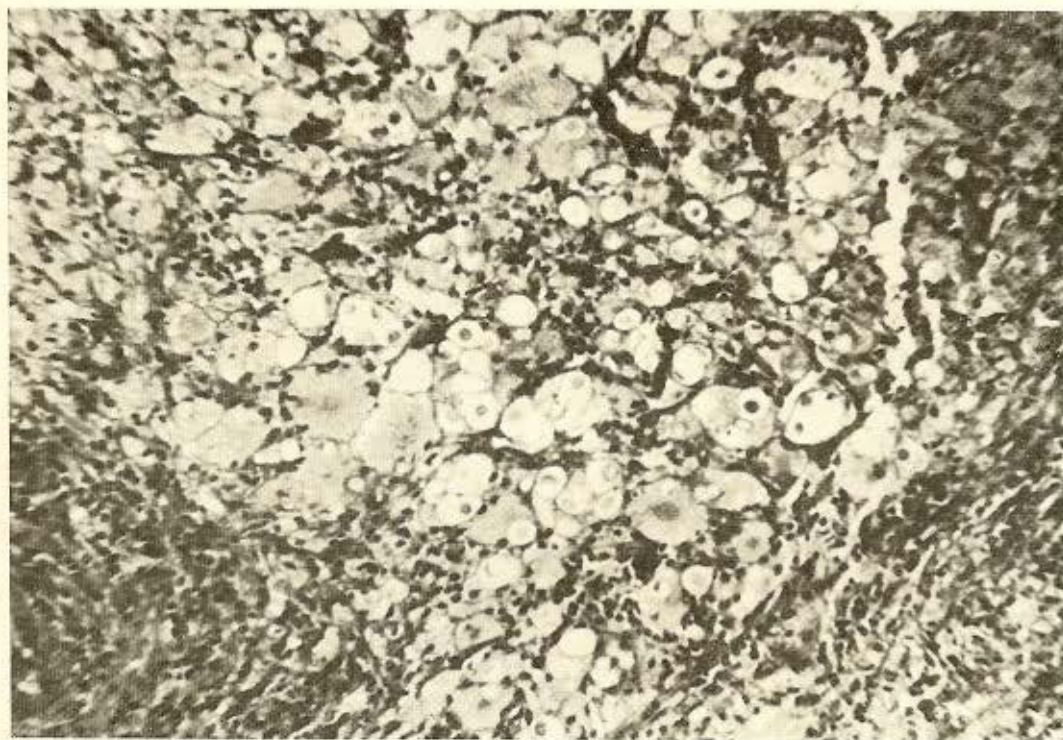


Fig. 4 — Lung section showing fungus cells and macrophages filling the pulmonary alveoli. Hematoxylin Eosin. 150 x

infection in man. The lesions may disclose a wide variation, ranging from barely perceptible lesions to dense areas of diffuse bilateral infiltrations^{27, 21}. Small subpleural nodules have also been described^{21, 25}. Unlike pulmonary tuberculosis caseation necrosis and cavitation seldom occur. When discovered as isolated nodules in the lung parenchyma, the lesion may be erroneously taken as a neoplasm^{2, 8, 15, 21}. When multiple, the nodules may mimic a metastatic tumor²⁷.

Lung schistosomiasis complicating pulmonary cryptococcosis is a very unusual finding, even in endemic areas of this parasitosis. Although the anatomic lesions in schistosomiasis *mansoni* have been mainly confined to organs closely related to the portal venous system, such as the liver, spleen and intestines, eggs and even adult worms may be carried through the pulmonary circulation where they become impacted in the small

arteries and arterioles. Discrete distribution of eggs through the pulmonary circulation is of no clinical or pathologic significance¹⁰. However, in special cases, the massive embolization of *Schistosoma mansoni* eggs may give rise to either focal^{9, 13, 16} or widespread arteritis^{12, 29} caused by the reaction around ova trapped in the pulmonary circulation which may lead to an obliterative cardiopulmonary syndrome^{13, 28, 32}. Focal consolidation areas in the lung parenchyma mainly around eggs and worms can also be observed in the lung parenchyma¹⁰. Amphotericin B has been the chemotherapeutic agent of choice for the treatment of cryptococcosis. Since the introduction of this drug, many cases had their progress interrupted by temporary remissions. Definite cures have been claimed, although longer observation periods are still necessary for a better evaluation of the results. Pulmonary cryptococcosis has been treated by amphotericin alone

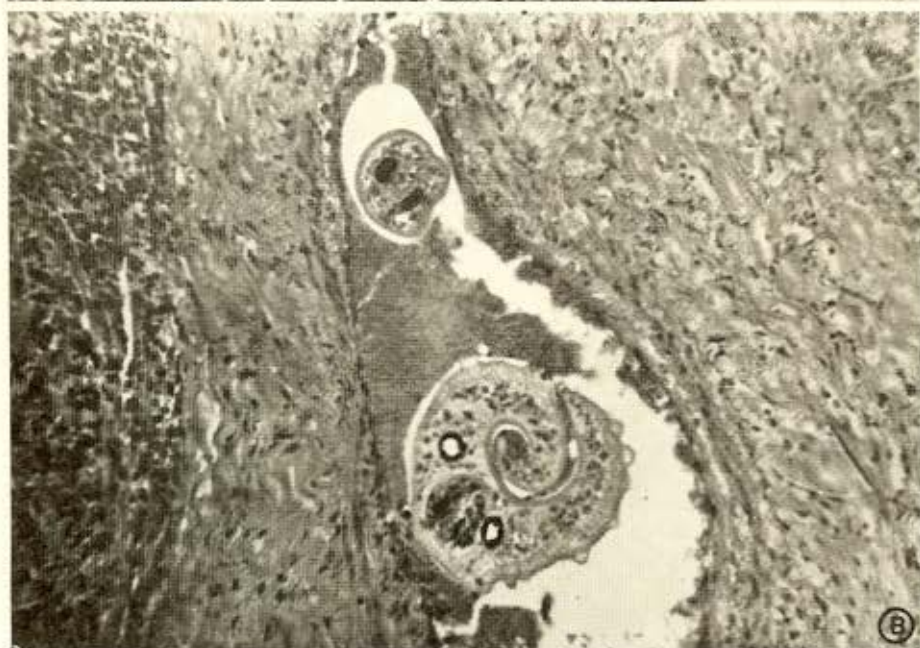
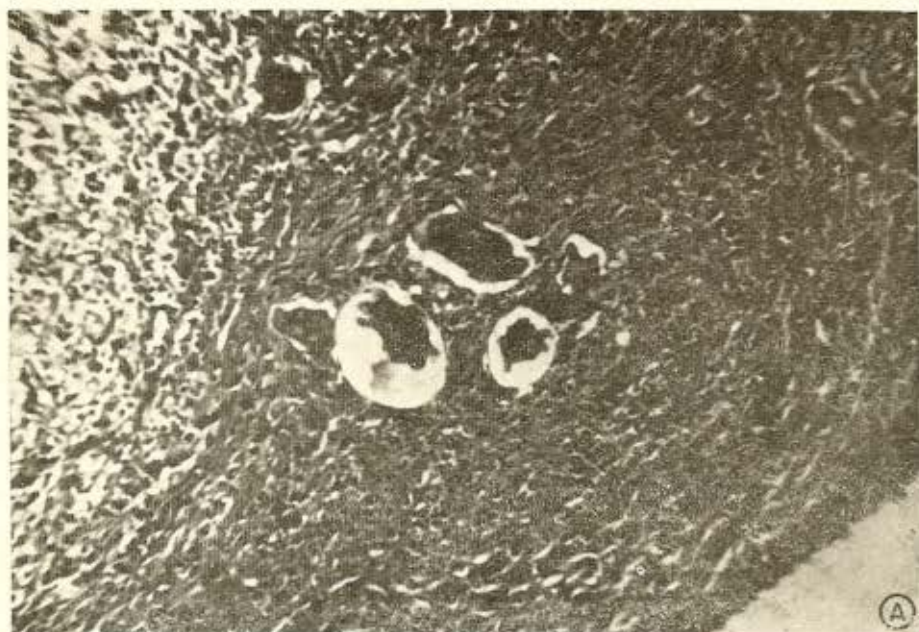


Fig. 5A) — *Schistosoma mansoni* eggs surrounded by dense fibrocollagenous reaction. Hematoxylin Eosin. 450 ×

Fig. 6B) — Adult worms of *S. mansoni* within a dilated pulmonary vessel. Hematoxylin Eosin. 450 ×

or in combination with surgical resection. In unilateral localized pulmonary cryptococcosis good results have been achieved from resection alone⁷. In cases with bilateral pulmonary disease the treatment with Amphotericin B is highly recommended.

In cryptococcal meningitis the Amphotericin has been reasonably effective^{3, 19, 33}. Eventual progression of the meningitic process was seen to be interrupted by temporary remissions in untreated patients⁶. However, many cases judged "cured" by the Amphotericin B administration are soon followed by a recurrence of the illness, and according to BUTLER et al.⁶ this sequence may be repeated two, three or even four times. This, according to those Authors would be in keeping with the finding that in many patients the cerebro-spinal fluid cell count and protein values remain abnormal for an extended period of time after treatment.

In meningeal cryptococcosis the combination of the intravenous and intra-theal Amphotericin B administration has resulted in improvement of the treatment. Patients treated in this way have experienced fewer relapses than those who have received the drug by intravenous route alone⁶.

RESUMO

Criptococose pulmonar e meníngea associada à esquistossomose pulmonar

Os Autores apresentam um caso de criptococose pulmonar, manifestando-se clinicamente como uma lesão solitária (toruloma), densa e localizada no terço superior do pulmão direito e que foi tratada mediante ressecção cirúrgica. Numerosos *Cryptococcus neoformans* foram observados no parênquima pulmonar, envolvidos por densa reação histiocítica. Coexistindo com a lesão produzida pelo fungo, foi observado grande número de ovos e vermes adultos de *Schistosoma mansoni* determinando arterite focal e áreas de consolidação pneumônica. O paciente desenvolveu posteriormente a forma meningo-encefálica da criptococose, tendo sido o *Cryptococcus neoformans* largamente demonstrado no líquido cérebro-espinhal. O tratamento complementar consistiu na administração de anfotericina B por via intravenosa e intra-tecal

o qual resultou no desaparecimento do quadro meningo-encefálico. Como seqüelas neurológicas foram observadas atrofia do nervo ótico, oftalmoplegia e surdez, seis meses após o tratamento quimioterápico.

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Recebido para publicação em 6/7/1971.