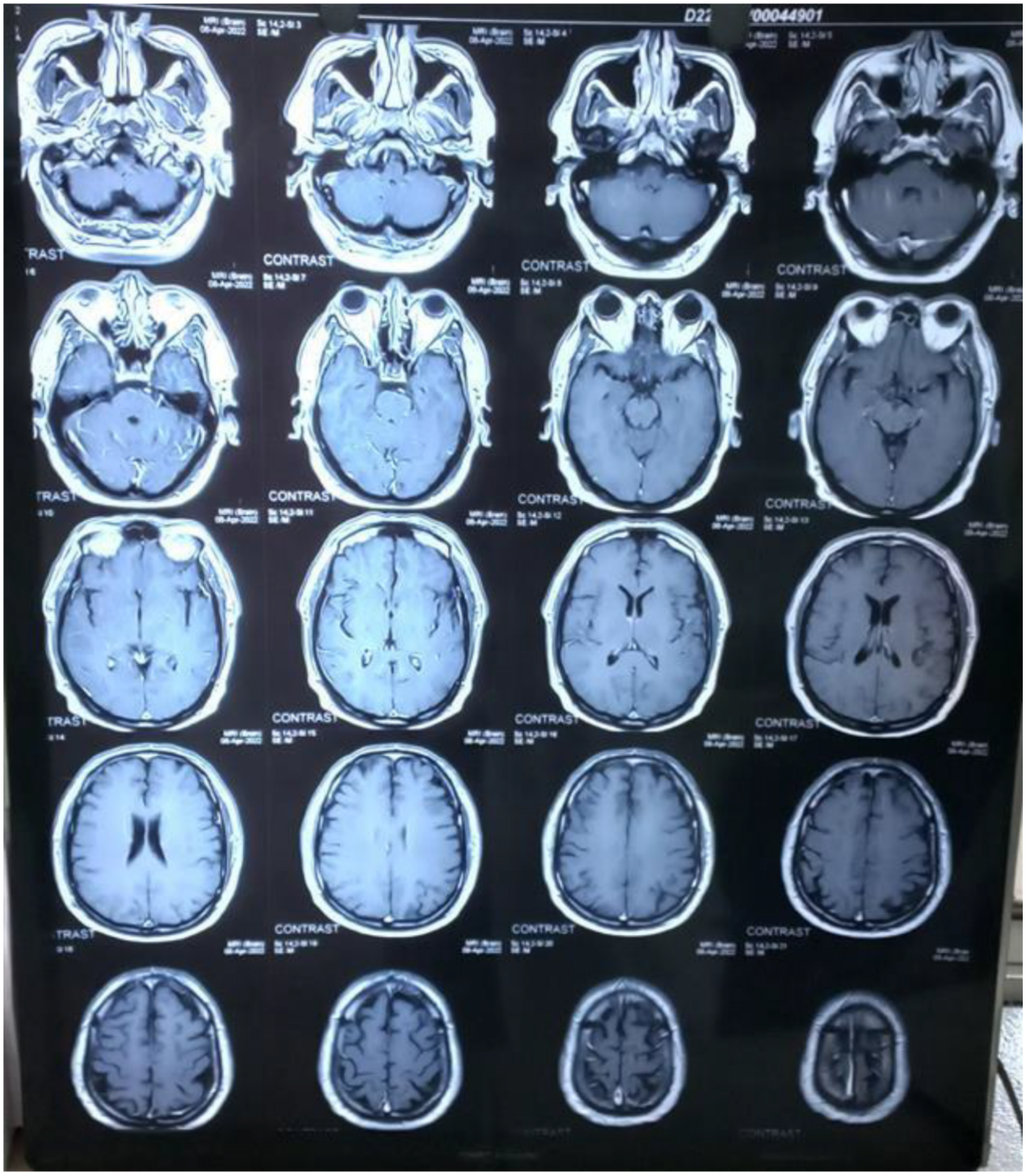

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Predictors of adverse outcome in sarcoidosis complicated by chronic pulmonary aspergillosis

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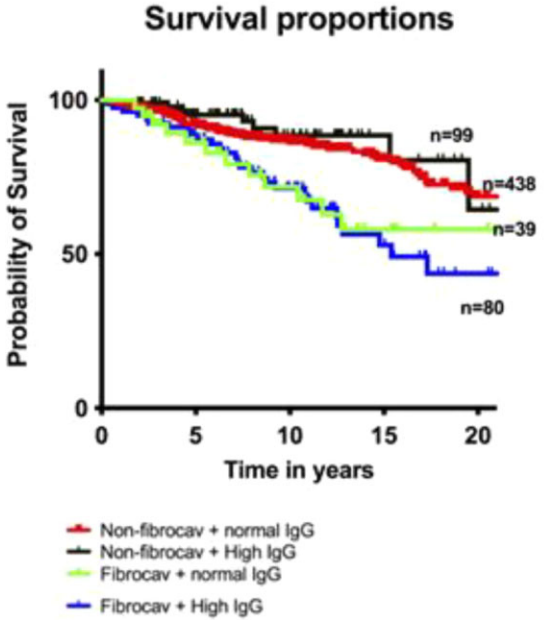
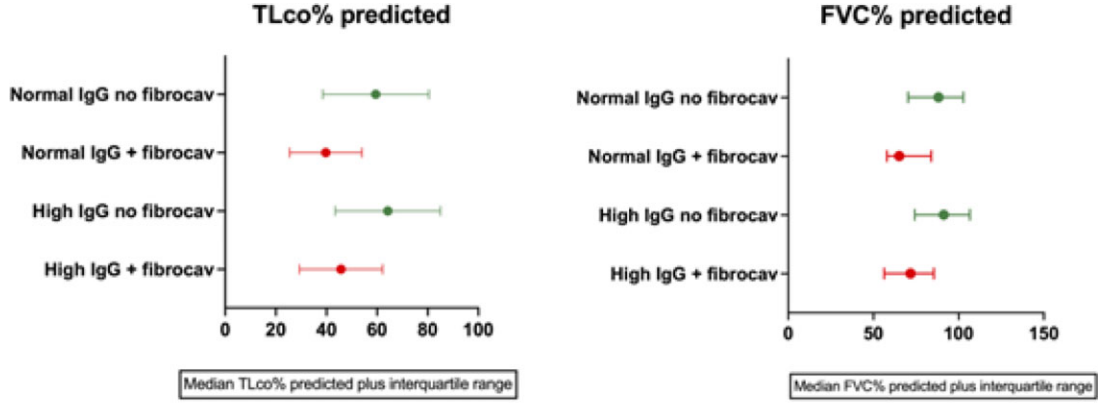
Introduction: Aspergillosis complicating pulmonary sarcoidosis is associated with high mortality.[1] The specific prognostic impact of fibrocavitary sarcoid disease, however, remains poorly understood. A better understanding of the factors that determine adverse outcomes in such patients may improve the management of both the underlying sarcoid disease and associated secondary fungal infection.

Methods: We implemented a clinical informatics pipeline to data-mine the hospital's clinical data warehouse and identify patients for inclusion in this study. Cases of pulmonary sarcoidosis with elevated *Aspergillus* IgG (>40 mgA/l) presenting between January 2009 and March 2021 were retrospectively identified. Controls (sarcoidosis with normal *Aspergillus* IgG titer) were case matched by baseline percentage-predicted gas transfer factor (TLco; ±5% variance). CPA cases were identified by using ISHAM criteria for diagnosing CPA, that is *Aspergillus* IgG >40 mgA/l plus keyword search for cavities or fungal ball in the CT reports based on search terms for aspergilloma, cavity, intra-cavitary, and mycetoma. Computed tomography (CT), baseline lung function, and survival data were analyzed.



	Fibrocavitary sarcoidosis		Non-fibrocavitary sarcoidosis	
	Normal *Asp* IgG	High *Asp* IgG	Normal *Asp* IgG	High *Asp* IgG
Total (N)	39	80	438	99
Survived (n)	26	50	366	90
Died (n)	13	30	72	9
% died	33.3	60	16.4	9.1
Median age at death	59*	56*	66*	63*

* P<0.01 (1-way ANOVA)



• Kruskal-Wallis test: "Do the medians vary signif. (P < 0.05)?" Yes

Results: Among 179 cases (high *Aspergillus* IgG) and 477 controls (normal *Aspergillus* IgG), no inter-group difference was evident in the median age at presentation [48 (IQR 40-58) vs 50 (IQR 42-59)] or gender (proportion female: 45.5% vs 51.1%). Amongst the cases, 80/179 (45%) had fibrocavitary changes, compared with 14/477 (2.9%) of the controls (P <.001). Radiologically-evident aspergilloma was present in 80% (64/80) of the cases with fibrocavitary sarcoidosis. Evidence of fibrocavitary destruction was associated with higher overall mortality (60% vs 9.1% in the non-fibrocavitary subgroup; <.0001), and poorer median survival (Fig. 1). The median age at death was lower where there was fibrocavitary disease, and even lower with high *Aspergillus* IgG, and this was statistically significant. These cases also had poorer lung function compared to non-fibrocavitary disease (Fig. 2): mean %-predicted forced vital capacity (FVC) 71.3% vs 91.4% (P <.0001), and in the controls: 69.9% vs 86.0% (P <.01). A similar trend was observed in %-predicted TLco amongst the fibrocavitary cases: 45.8% vs 64.2% non-fibrocavitary (P <.0001) and in the fibrocavitary controls: 39.7% vs 59.0% non-fibrocavitary (P <.0001). Comparing only those with fibrocavitation, neither the percentage-predicted FVC (71.3% vs 69.9% predicted; P = .82) nor the percentage-predicted TLco (45.7% and 39.7% predicted; P = .16) differed between cases and controls.

Conclusions: Fibrocavitary sarcoidosis is associated with worse lung function and poorer median survival. In this group, elevated *Aspergillus* IgG highlights a greater incidence of aspergilloma.

Implications: Fibrotic transformation of pulmonary sarcoidosis heightens symptom burden, predisposes to chronic *Aspergillus* infection, and is prognostically important particularly when there is supervening fibrocavitary lung destruction. Sensitive stratification of such patients for the long-term outcomes may help identify particular individuals for earlier and more focused therapeutic intervention.

Sources:

1. Uzunhan *et al*., Chronic pulmonary aspergillosis complicating sarcoidosis, European Respiratory Journal 2017 49: 1 602 396; DOI: 10.1183/13993003.02396-2016

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Disseminated Histoplasmosis in a Ghanaian HIV Patient: Role of Urine Histoplasma Antigen Testing in Rapid Diagnosis

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Background: The inhalation of the thermally dimorphic fungus Histoplasma capsulatum, may result in a wide spectrum of clinical manifestations, ranging from asymptomatic to acute or chronic pulmonary infection to disseminated infection. Symptomatic infections usually occur with high-level exposures or in immunocompromised patients mainly people with HIV. Despite the improved access to antiretroviral therapy, HIV-associated histoplasmosis remains a significant opportunistic infection in endemic regions including Africa. Unfortunately, histoplasmosis is rarely on the diagnostic radar of clinicians in several African countries such as Ghana due to insufficient awareness, inadequate epidemiological data, and poor fungal diagnostic capacity. Herein, we present a case of disseminated histoplasmosis in an HIV/AIDS patient in a tertiary hospital in Ghana.

Case Presentation: Clinical history: A 43-year-old female was referred to the Dermatology Clinic of the Komfo Anokye Teaching Hospital (KATH) with symptoms of fever, cough, and anorexia. She had a history of a skin rash six weeks prior, which initially began on her face and later spread to the trunk and extremities. She was a known HIV/AIDS patient on anti-retroviral drugs (EFV, TFV, 3TC) with no other chronic conditions. She was anemic with a previous hemoglobin level of 7.6 g/dl. Initial diagnostic workup for cutaneous bacterial or viral infection detected no abnormality.

Examination: She was semi-conscious, and her nostrils were clogged with crust. The patient appeared pale, warm, and anicteric. The face, trunk, and extremities (including palms) were covered with mucocutaneous erosions, ulcers, multiple papule plaques, and nodules. Examination of the cervix revealed the presence of lymph nodes.

Investigations: A fungal diagnostic work-up was done to rule out cutaneous or disseminated mycosis particularly cryptococcosis which was previously captured as a differential diagnosis. Serum cryptococcal antigen lateral flow assay (LFA) (CrAg LFA, IMMY) and *Aspergillus galactomannan* (GM) (sona *Aspergillus* GM LFA, IMMY) tests were both negative, but urine Histoplasma GM enzyme immunoassay (EIA) (clarus Histoplasma GM EIA, IMMY) test was positive with a very high optical density indicating high fungal burden was reported. A skin biopsy was also sent for histopathology and fungal culture. Histopathology analysis revealed the presence of yeast cells with round central nuclei and cytoplasmic clearing. Special staining with Periodic acid–Schiff (PAS) confirmed the presence of yeast cells, suggestive of histoplasmosis. Fungal culture was however negative after 8 weeks of incubation. A diagnosis of disseminated histoplasmosis was made.

Treatment and outcome: The patient was administered 200 mg bid of itraconazole. Few weeks after treatment, most of her skin lesions and ulcers were healed. The patient was discharged on itraconazole after the disappearance of some of her lesions. Few weeks later, the patient was admitted but died due to complications of anemia.

Conclusion: Disseminated histoplasmosis in HIV may be a relatively common but largely unrecognized condition in Ghana. This case report highlights the need to improve awareness of histoplasmosis among clinicians in Ghana and enhance laboratory capacity to provide timely simple contemporary fungal tests for rapid diagnosis and prompt initiation of effective antifungal agents.