

Chronic pulmonary aspergillosis as a cause of smear-negative TB and/or TB treatment failure in Nigerians

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SUMMARY

OBJECTIVE: To evaluate chronic pulmonary aspergillosis (CPA) as an alternative diagnosis of smear-negative tuberculosis (TB) and treatment failure in TB patients in Nigeria.

METHODS: We conducted a cross-sectional multicentre survey in human immunodeficiency virus (HIV) positive and negative adult patients at the end of their TB treatment in clinics in Lagos and Ilorin states. All were assessed using clinical examination, chest X-ray (CXR) and aspergillus immunoglobulin G (IgG) serology, and some for sputum fungal culture. CPA was defined as a positive *Aspergillus fumigatus* IgG titre with compatible CXR or a positive sputum culture of *Aspergillus* with a visible fungal ball on CXR with symptoms of underlying lung disease.

RESULTS: Of 208 patients recruited between June 2014

and May 2015, 153 (73.6%) were HIV-positive. The mean age was 39.8 years, 124 (59.6%) were female and 39 (18.8%) were unable to work. The median CD4 count was 169.5 cells/ml (range 4–593) in HIV-infected patients with positive *Aspergillus* IgG. Overall, 109 (52.4%) had documented TB, 140 (67.3%) had a productive cough and 50 had haemoptysis. CPA prevalence was 8.7%; 10 (6.5%) had HIV infection and 8 (14.5%) were HIV-negative (Fisher's exact $P = 0.092$).

CONCLUSION: CPA is a neglected disease in Nigeria, and most cases match the World Health Organization diagnostic criteria for smear-negative TB.

KEY WORDS: aspergillosis; tuberculosis; HIV; chronic pulmonary aspergillosis; aspergillus serology

CHRONIC PULMONARY ASPERGILLOSIS (CPA) is a progressive pulmonary disease that can complicate several other respiratory disorders, such as tuberculosis (TB), and which affects an estimated 3 million people worldwide.¹ A history of pulmonary disorders is almost universal in CPA patients.² The global prevalence of CPA secondary to TB is estimated to lie between 0.8 and 1.37 million cases, with 43 cases per 100 000 population in Congo and Nigeria.³ CPA is associated with significant morbidity and mortality. Long-term oral antifungal treatment is given due to the high risk of relapse.² Resistance or intolerable side effects occur in up to 50% of patients.⁴ Studies of aspergillomas in Taiwan, South Korea, China and India have identified TB as the aetiological factor in up to 93% of cases of CPA.^{5–8} A survey in the United Kingdom found that of 544 patients left with a residual cavity of 2.5 cm at 1 year after anti-tuberculosis treatment, 36% had positive *Aspergillus* antibodies and 22% had an

aspergilloma after 3 years.^{9,10} No similar surveys have been reported since.

TB is more common in Africa than in other continents,¹¹ and has a clear relationship with HIV/AIDS (human immunodeficiency virus/acquired immune-deficiency syndrome). This raises the possibility that CPA is much more common in Africa. The first case of CPA in Africa was an aspergilloma in a South African farmer in 1965.¹² Subsequent cases of CPA have been documented in the Ivory Coast,¹³ Senegal,¹⁴ Ethiopia,¹⁵ Nigeria,¹⁶ and more recently in Uganda¹⁷ and Tanzania.¹⁸ A South African report revealed a 9.9% rate of aspergillomas in patients with life-threatening haemoptysis in an area of high TB incidence.¹⁹ Currently, many CPA cases are either diagnosed late or misdiagnosed.

Here, we evaluated CPA as a cause of smear-negative TB and/or anti-tuberculosis treatment failure in HIV-positive and -negative Nigerians.

METHODOLOGY

Study population

Patients were enrolled in a cross-sectional study conducted at three centres in Nigeria: the National Institute for Medical Research ART and TB clinic, Lagos; DOTS clinics at Lagos University Teaching Hospital, Lagos; and the University of Ilorin Teaching Hospital, Ilorin. HIV-positive and -negative adults who were in their last month of anti-tuberculosis treatment (smear + Xpert-positive; Xpert® MTB/RIF, Cepheid, Sunnyvale, CA, USA) or being treated for 'smear-negative TB' (based on radiological and clinical pictures) were recruited. Two control groups were included: 50 blood donors and 50 HIV-positive patients on ART with CD4 count > 350 cells/ml and without a history of TB. Controls underwent venepuncture only.

Ethical approval was obtained from the institutional ethics committees of the study site hospitals. Written informed consent was provided by each participant.

Study design

Over a 12-month period from June 2014 to May 2015, 208 patients and 100 controls (153 HIV-positive patients and 55 HIV-negative patients) were recruited. All were assessed clinically and using chest X-ray (CXR) and *Aspergillus* immunoglobulin (Ig)G serology. Clinical examination included chest auscultation and testing of blood oxygen levels. If patients had a productive cough, sputum was collected and processed for microscopy and fungal culture. Five millilitres of blood was obtained from all participants. CXRs were assessed by two independent consultant radiologists.

Data collection

A questionnaire was used to collect basic sociodemographic data, clinical parameters and medical history. Other pertinent data such as drug history, latest CD4 count (within last 6 months) and HIV serology status were obtained.

Laboratory processing

Serum was transferred in dry ice to the Mycology Reference Centre, Manchester, UK. Levels of *Aspergillus fumigatus*-specific IgG antibodies were measured using an ImmunoCAP® system (ThermoFisher Scientific, Waltham, MA, USA). An IgG level > 40 mg/l was considered elevated.

Definitions

CPA was diagnosed based on the criteria proposed by Denning et al.,²⁰ and required the presence of: 1) underlying pulmonary disease, 2) symptoms, 3) radiological findings, and 4) microbiological evidence of aspergillosis, *A. fumigatus* IgG antibody-positive

or culture from sputum of a non-*fumigatus* species of *Aspergillus* in patients with a fungal ball visible on CXR. Pulmonary TB was diagnosed if a patient had a positive sputum smear test for acid-fast bacilli or a positive Xpert 2110 polymerase chain reaction (PCR) test.

Anti-tuberculosis treatment failure was diagnosed in patients who were sputum smear-positive at 5 months after the initiation of anti-tuberculosis treatment or in persistently symptomatic patients in the last 1 month of treatment. A patient was described as 'symptomatic' if he/she had at least one of haemoptysis, cough, productive cough and severe fatigue. CXR features indicative of CPA were at least one of cavitation, fungal ball, pleural thickening or fibrosis. An unspecified fungal ball was diagnosed in patients with an apparent aspergilloma on CXR, but with normal *Aspergillus* IgG levels.

Data analysis

Analyses were performed using SPSS v22 (IBM, Armonk, NY, USA) and a 5% significance level was used. Summary statistics were presented using frequencies and percentages for binary and categorical variables, mean values and standard deviations for normally distributed continuous variables, and median values and interquartile ranges (IQRs) for non-normally distributed continuous variables. Natural logarithm transformations were used to perform analyses on non-normally distributed variables.

χ^2 and Fisher's exact tests were employed to compare proportions between groups, and Student's *t*-tests were used to compare means. Linear regression was used to assess the relationship between continuous variables.

RESULTS

Of the 208 patients recruited into the study, 153 (73.6%) were HIV-positive and 55 (26.4%) were HIV-negative. Ninety-five (95/141, 67.4%) were undergoing anti-tuberculosis treatment for the first time, whereas 46 (32.6%) were on a retreatment regimen, having been diagnosed as having failed treatment. Thirty-nine (18.8%) were unable to work due to the severity of their illness. There were 124 (59.6%) females, of whom 52 (41.9%) were aged 30–39 years. The mean age of the participants was 39.8 years (standard deviation 12.3, range 16–82). Ninety-nine (64.7%) of those HIV-infected were in the age group 30–49 years and 25 (16.3%) in the 10–29 years age group. The median CD4 count was 212.5 ($n = 136$, IQR 88.5–337.5) in HIV-infected patients and 169.5 ($n = 8$, range 4–593) in HIV-infected patients with positive *Aspergillus* IgG. One hundred and nine patients (52.4%) had TB and 140 (67.3%) had a productive cough. The median duration of cough among the study population was 3 months ($n = 120$,

Table Relationship between smear status and clinical features in HIV-positive and -negative patients

Smear/Xpert	HIV-positive (n = 153)		P value	HIV-negative (n = 55)		P value
	With data (n = 100)			With data (n = 50)		
	Positive (n = 27) n/N (%)	Negative (n = 73) n/N (%)		Positive (n = 18) n/N (%)	Negative (n = 32) n/N (%)	
<i>Aspergillus</i> IgG-positive	2 (7)	7 (10)	>0.99	1 (6)	6 (19)	0.40
<i>Aspergillus</i> IgG titre, geometric mean (range)	6.0 (1.1–135.0)	6.8 (1.0–194.0)	0.66	9.3 (1.0–159.0)	11.9 (1.0–186.0)	0.52
Age, years, mean \pm SD	40.6 \pm 11.6	39.6 \pm 10.4	0.70	42.7 \pm 17.6	42.5 \pm 13.8	0.98
Symptoms						
Marked haemoptysis	0	1/70 (1)	>0.99	2 (11)	5/23 (22)	0.44
Fatigue	11 (41)	33/72 (46)	0.65	12 (67)	11/20 (55)	0.46
Productive cough	12 (44)	48/72 (67)	0.044	16 (89)	19/25 (76)	0.43
Chest pain	8/26 (31)	20 (27)	0.74	7 (39)	15/20 (75)	0.024

HIV = human immunodeficiency virus; IgG = immunoglobulin G; SD = standard deviation.

IQR 1–8, range 1–96). Positive sputum cultures for *Aspergillus* spp. were obtained in 28 (20%), *A. fumigatus* in 15, *A. flavus* in 10 and *A. niger* in 3. Fifty patients had haemoptysis, nine with moderately severe frank haemoptysis.

Serology results, chronic pulmonary aspergillosis and risk factors

Seventeen (8.2%) patients had a positive *Aspergillus* IgG above the 40 mg/l cut-off point. The median titre was 6.2 mg/l (IQR 3.7–14.3, range < 2–194). As both CD4⁺ and *Aspergillus* IgG levels were positively skewed, log transformations were performed to allow a linear regression to be used to determine their statistical relationship; this was not significant. A smear/Xpert result was available for 150 patients; the remaining 58 patients were diagnosed by CXR. In the HIV-positive subgroup, there was no significant difference in the proportion of IgG-positive patients between patients with confirmed (smear and/or Xpert) TB and smear-negative patients (2/27, 7.4% vs. 7/73, 9.6%; Fisher's exact $P > 0.99$). Similarly, in the HIV-negative subgroup, there was no significant difference in the proportion of IgG-positive patients with confirmed TB and smear-negative patients (1/18, 5.6% vs. 6/32, 18.8%; Fisher's exact $P = 0.40$; Table).

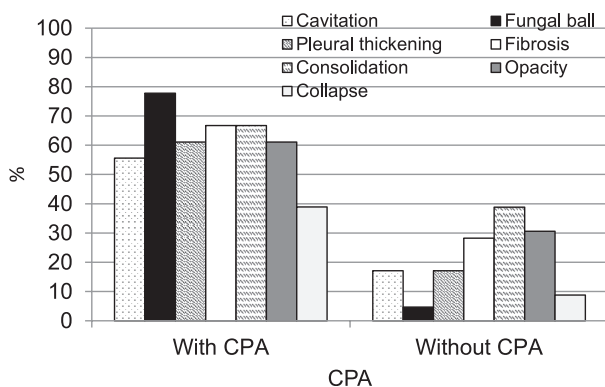


Figure 1 Proportion with radiological features in IgG-positive and -negative patients. CPA = chronic pulmonary aspergillosis; IgG = immunoglobulin G.

However, there was a significant difference in the geometric mean of *Aspergillus* IgG concentration between the HIV-infected and non-HIV-infected patients (6.0 vs. 10.6 mg/l; $P = 0.002$). None of the controls had *Aspergillus* IgG levels above the threshold.

Using the definition of CPA, 18/208 patients (8.7%) had CPA, including three with *Aspergillus* IgG < 40 mg/l who had fungal balls on CXR and grew *A. niger* ($n = 2$) and *A. flavus* ($n = 1$) in their sputum. A greater proportion of HIV-negative than HIV-positive patients had CPA (8/55, 14.5% vs. 10/153, 6.5%; Fisher's exact $P = 0.092$). In the 'treatment failure' group, seven had CPA, only one of whom was undergoing anti-tuberculosis treatment for the first time. In the HIV-positive subgroup, there was no significant difference ($P = 0.74$) in the CD4 count between those with CPA ($n = 9$, geometric mean 162.5) and those without CPA ($n = 127$, geometric mean 182.4). A greater proportion of patients with CPA than those without CPA had chest pain, although the difference was not significant (10/17, 58.8% vs. 63/174, 36.2%; $P = 0.067$).

Radiological findings

The proportions of different radiological features were for the most part similar for the whole group and the HIV-positive subgroup (Figures 1–3): 79 (46.5%) patients without CPA had a normal CXR, 84.8% (67/79) of whom were HIV-positive and 52.2% had CD4 count < 250 cells/mm³; none had *Aspergillus* IgG above 40 mg/l. All nine HIV-positive patients with *Aspergillus* IgG > 40 mg/l had radiological features suggestive of CPA; six of eight with a documented result had a CD4 count of < 250 cells/mm³.

Ten of 18 (55.6%) patients with CPA had cavitation compared with 17.1% (29/170) of the patients without CPA (Appendix Table A).^{*} Of 18 patients with CPA, 14 (77.8%) had a fungal ball,

^{*} The appendix is available in the online version of this article, at <http://www.ingentaconnect.com/content/ijuatld/ijtd/2017/00000021/00000009/art00018>

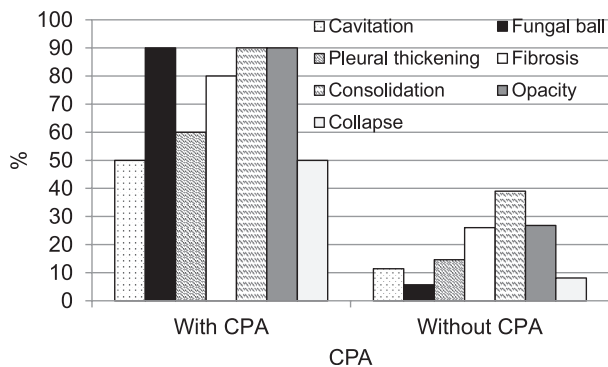


Figure 2 Proportion with radiological features in those with and those without CPA for HIV-positive patients. CPA = chronic pulmonary aspergillosis; HIV = human immunodeficiency virus.

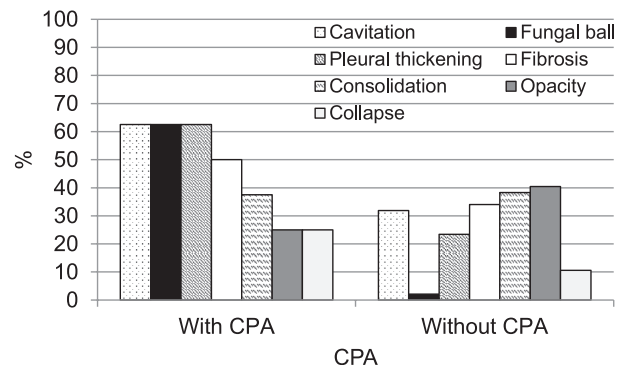


Figure 3 Proportion with radiological features in those with and those without CPA for HIV-negative patients. CPA = chronic pulmonary aspergillosis; HIV = human immunodeficiency virus.

compared with 4.7% (8/170) without CPA; 61.1% (11/18) of those with CPA had pleural thickening compared with 17.1% (29/170) of those without CPA. Fibrosis was observed in 12/18 (66.7%) of those with CPA compared with 28.2% (48/170) without CPA. Overall, 90.0% (9/10) of patients with CPA had a fungal ball compared with 5.7% (7/123) of those without CPA, 60.0% (6/10) of CPA patients had pleural thickening compared with 14.6% (18/123) of those without CPA ($P=0.002$, Fisher's exact), and 80.0% (8/10) of CPA patients had fibrosis compared with 26.0% (32/123) of those without CPA ($P=0.001$, Fisher's exact) (Appendix Figures A.1–A.4). No formal statistical testing was performed for these four radiological features, as they were part of the definition of CPA. There were significant differences between the CPA and non-CPA patients in the proportion with consolidation (12/18, 66.7% vs. 66/170, 38.8%; $P=0.023$), opacity (11/18, 61.1% vs. 52/170, 30.6%; $P=0.009$), collapse (7/18, 38.9% vs. 15/170, 8.8%; $P=0.002$), air crescent/Monod sign (4/18, 22.2% vs. 9/170, 5.3%; $P=0.025$), pleural effusion (4/18, 22.2% vs. 11/170, 6.5%; $P=0.041$), calcification (4/18, 22.2% vs. 8/170, 4.7%; $P=0.018$) and hilar lymphadenopathy (5/18, 27.8% vs. 14/170, 8.2%; $P=0.023$). These features were also significant in the HIV-positive subgroup (Appendix).

Eight cases of an 'unspecified' fungal ball were diagnosed with apparent aspergilloma on CXR: six of these patients had normal *Aspergillus* IgG levels and negative sputum cultures but some symptoms, and two patients had *Aspergillus* IgG levels above the cut-off and no symptoms.

DISCUSSION

The African Region accounts for about four out of every five HIV-positive TB cases and TB deaths among people who are HIV-positive.²¹ Nigeria ranks fifth among the 22 high TB burden countries,²² and CPA is a known complication of TB.²³ Even when

treated, CPA has a short-term mortality of 20–33% and a mortality over 5 years of 50%.²³ The estimated prevalence of CPA in TB patients in Nigeria is 42.9/100 000, but this estimate is an extrapolation that requires confirmation.²³ Furthermore, there are no published studies of CPA in HIV-positive patients.

In this multicentre study, we confirmed the presence of CPA among patients being managed for TB in Nigeria, with an overall prevalence of 8.7%. However, this overall figure obscures a proportion that is nearly twice as high in HIV-negative patients (14.5%), compared with HIV-positive patients (6.5%). A report from Iran gave a prevalence of 13.7%, very similar to our findings, as they excluded HIV-infected TB patients,²⁴ and similar to data from Japan (16.7%).²² A possible explanation for the marked difference between HIV-infected and non-HIV-infected patients is that HIV patients might not be able to mount a sufficient antibody response during *Aspergillus* infection, especially those with low CD4 counts, as observed in the present study.

In 2014, pulmonary TB in Nigeria was reported in 100 000 patients with HIV infection and 470 000 without HIV infection.²¹ However, only 22 000 with HIV infection survived, compared with 300 000 who were not HIV-infected. Applying the rates of CPA that we found, we could anticipate an annual incidence of ~1430 HIV-positive CPA cases and ~43 500 HIV-negative CPA cases. Assuming a 15% annual mortality or lobectomy (cure) rate, we anticipate a 5-year period prevalence of 141 619 CPA cases, substantially greater than the first estimate of 60 383,²³ but close to our more recent estimate of 120 753.²⁵ While the HIV patients were not selected for any particular characteristic, we did explicitly study several smear-negative, HIV-negative patients with continuing symptoms. Over 50% of the patients met the criteria for anti-tuberculosis treatment failure: 67 were in their last month of treatment and were still symptomatic and 46 were undergoing retreatment for TB. Extrapolation to the whole HIV-negative population may therefore lead to overesti-

mation, but conversely we omitted the two patients with probable simple aspergillomas from this calculation.

We measured *A. fumigatus* antibodies because *A. fumigatus* is the most commonly implicated *Aspergillus* spp., accounting for over 90% of aspergillosis in Europe.^{26,27} However, a recent report from South-Western Nigeria using PCR revealed that *A. fumigatus* only accounted for 57.1% of clinical and environmental isolates, followed by *A. niger*, at 28.6% and *A. flavus*, at 7.4%.²⁸ In an earlier study from Eastern Nigeria, *A. fumigatus* represented 51.9%, *A. niger* 33.3% and *A. flavus* 14.8%.²⁹ In Northern Nigeria, Kwanashie et al. found that *A. fumigatus* accounted for 52.4%, *A. flavus* 21.9%, and *A. niger* 11.4%.³⁰ *A. fumigatus* antibody assays may have poor sensitivity for infection with other *Aspergillus* species.³¹ This might account for the three patients who were finally diagnosed with CPA who had *Aspergillus* IgG < 40 mg/l, but with positive sputum cultures for *A. niger* ($n=2$) and *A. flavus* ($n=1$). However, as culture also has low sensitivity, this is likely an underrepresentation of the true estimate of the disease in an area where up to 40% of clinical *Aspergillus* species are non-*fumigatus*.

Conventional CXR is the imaging modality used for the initial evaluation of patients with pulmonary complications in low- and middle-income countries (LMICs). However, it has limited sensitivity and specificity compared with computed tomography (CT), especially in immunocompromised patients.³² We found that 43.8% of HIV-positive study patients had a normal CXR, despite being managed for TB—consistent with reports from other studies (20–50% of bacteriological confirmed cases).^{7,33} It is possible that all abnormal features returned to normal or were normal previously. CXR does not distinguish between pulmonary TB and CPA, as cavities and fibrosis are seen in both.^{34,35} There are no published data documenting the post-treatment CT appearances of pulmonary TB in HIV-positive patients; however, cavitation has been observed in 21–23% of HIV-negative African patients.²³ There is a need for a predictive model that will help to increase the index of suspicion of CPA among clinicians in LMICs.

We found 22 patients with fungal balls, including 14 (63.6%) who had CPA. A further eight patients had an unspecified fungal ball without either symptoms or positive *Aspergillus* IgG. This could have been due to over-reading of compound shadows in the lung apex, a problem that would be resolved with CT. Haemoptysis is a known presentation of pulmonary aspergillomas, with associated morbidity and mortality.¹⁹ Frank haemoptysis was observed in nine patients, similar to the frequency found in another study among TB patients with aspergillomas.¹⁹ Haemoptysis from aspergillomas in Nigeria has been associated with high mortality (37.5%) despite

surgical intervention.¹⁶ This life-threatening condition could be pre-empted by earlier diagnosis.

Limitations of this study included a lack of follow-up of the study population; serial CXRs were not performed to document progression or later development of disease. Furthermore, only one centre performed Xpert testing at the time of the study. To exclude comorbidity, no patients on second-line anti-tuberculosis treatment being managed for multidrug-resistant TB were recruited.

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Potential conflicts of interest: DWD and his family hold Founder shares in F2G Limited, a University of Manchester spin-out antifungal discovery company, in Novocyt which markets the Myconostica real-time molecular assays. He acts or has recently acted as a consultant to Astellas, Sigma Tau, Basilea, Scynexis, Cidara, Biosergen, Quintilles, Pulmatrix and Pulmocide. In the last 3 years, he has been paid for talks on behalf of Astellas, Dynamiker, Gilead, Merck and Pfizer. He is a longstanding member of the Infectious Disease Society of America Aspergillosis Guidelines group, the European Society for Clinical Microbiology and Infectious Diseases Aspergillosis Guidelines group and the British Society for Medical Mycology Standards of Care Committee.

ROO has been paid for talks on behalf of AstraZeneca and Pfizer in the last 3 years.

MDR acts a consultant for Gilead Science eEurope, Astellas, MSD, Pfizer and Basilea. He is a member of the European Society for Clinical Microbiology and Infectious Diseases Aspergillosis Guidelines writing groups.

The other authors have no conflicts of interest.

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APPENDIX

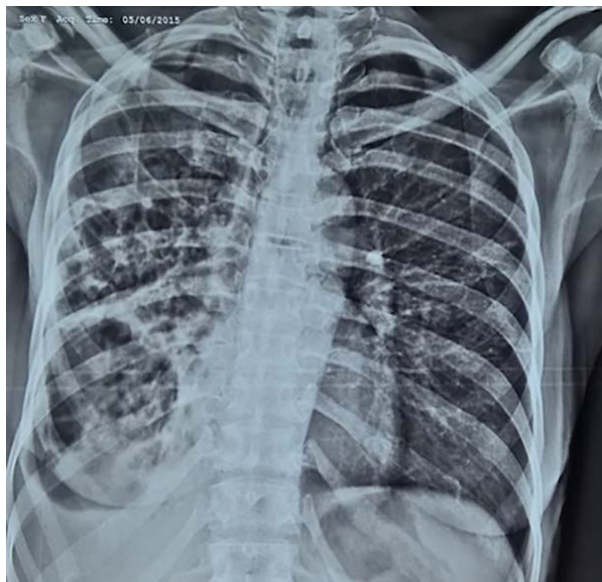


Figure A.1 Right fibrosis, cavities, large cavity, right pleural effusion and consolidation.



Figure A.2 Right fibrosis, right pleural effusion and consolidation.

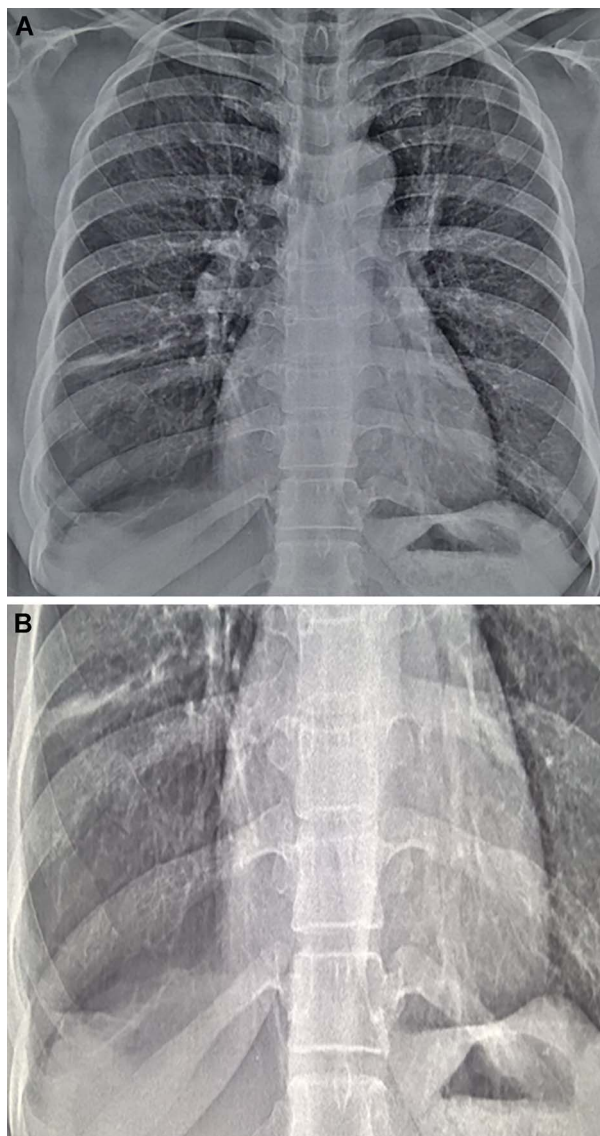


Figure A.3 **A)** Right pleural thickening, minor fissure and right costophrenic angle; **B)** magnified version of **A)** showing the thickened section.

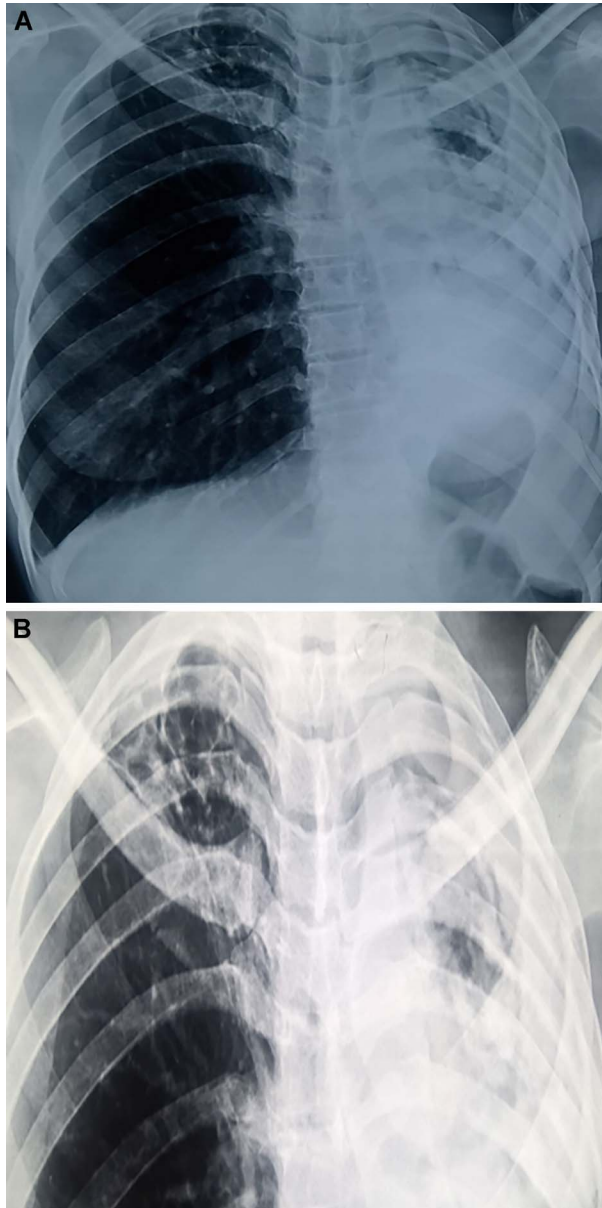


Figure A.4 **A)** Large cavity, fungus ball and halo or crescent sign (left upper zone), left segmented collapse, consolidation; **B)** magnified version of Figure 4.

Table A Distribution of radiological findings in relation to *Aspergillus* IgG serostatus, HIV status and haemoptysis in percentages (percentages indicate those with the characteristic specified in the row out of those with the characteristic specified in the column)

	Normal (n = 79) %	Consolidation (n = 78) %	Fibrosis (n = 60) %	Cavitation (n = 39) %	Fungal ball (n = 22) %	Pleural thickening (n = 40) %	HIV-positive (n = 153) %	HIV-negative (n = 55) %	<i>Aspergillus</i> IgG-positive (n = 17) %
Normal	100	0	0	0	0	0	43.8	21.8	0
Consolidation	0	100	83.3	53.8	63.6	72.5	37.3	38.2	58.8
Fibrosis	0	64.1	100	56.4	59.1	75.0	26.1	36.4	52.9
Cavitation	0	26.9	36.7	100	40.9	47.5	12.4	36.4	52.9
Fungal ball	0	17.9	21.7	23.1	100	25.0	10.5	10.9	76.5
Pleural thickening	0	37.2	50.0	48.7	45.5	100	15.7	29.1	52.9
HIV-positive	84.8	73.1	66.7	48.7	72.7	60.0	100	—	52.9
HIV-negative	15.2	26.9	33.3	51.3	27.3	40.0	—	100	47.1
Blood staining	22.8	24.4	30.0	30.8	45.5	25.0	20.9	32.7	47.1
Frank haemoptysis	3.8	3.8	6.7	7.7	4.5	5.0	1.3	12.7	5.9
<i>Aspergillus</i> IgG-positive	0	12.8	15.0	23.1	59.1	22.5	5.9	14.5	100

IgG = immunoglobulin G; HIV = human immunodeficiency virus.

RESUME

OBJECTIF : Evaluer l'aspergillose pulmonaire chronique (CPA) en tant que diagnostic alternatif de la tuberculose (TB) à frottis négatif et de l'échec du traitement de patients TB au Nigeria.

MÉTHODE : Nous avons réalisé une enquête transversale multicentrique chez des patients adultes positifs et négatifs au virus de l'immunodéficience humaine (VIH) à la fin de leur traitement de TB dans des centres de santé des états de Lagos et d'Ilorin. Tous les patients ont été évalués par un examen clinique, une radiographie pulmonaire (CXR) et une sérologie à la recherche d'immunoglobuline G (IgG) anti-*Aspergillus*, et certains patients pour une culture de crachats à la recherche d'une infection fongique. La CPA a été définie comme un titre positif d'IgG anti-*Aspergillus fumigatus* avec une CXR compatible ou une culture de crachats positive à *Aspergillus* avec une boule fongique visible sur la CXR et des symptômes de pathologie pulmonaire chronique.

RÉSULTATS : Des 208 patients recrutés entre juin 2014 et mai 2015, 153 (73,6%) ont été VIH positifs. L'âge moyen a été de 39,8 ans, 124 (59,6%) ont été des femmes et 39 (18,8%) ont été incapables de travailler. Le taux médian de CD4 a été de 169,5 cellules/ml (fourchette 4–593) chez les patients infectés par le VIH avec des IgG positives à *Aspergillus*. Au total, 109 (52,4%) avaient une TB documentée, 140 (67,3%) avaient une toux productive et 50 ont eu des hémoptysies. La prévalence de la CPA a été de 8,7% ; 10 (6,5%) patients avaient une infection à VIH et 8 (14,5%) patients ont été VIH négatifs (test exact de Fisher $P = 0,092$).

CONCLUSION : La CPA est une maladie négligée au Nigeria, correspondant souvent aux critères de diagnostic de l'Organisation Mondiale de la Santé de TB « à frottis négatif ».

RESUMEN

OBJETIVO: Evaluar la aspergilosis pulmonar crónica (CPA) como diagnóstico diferencial en los casos de tuberculosis (TB) con baciloscopia negativa y fracaso terapéutico en Nigeria.

MÉTODOS: Se llevó a cabo un estudio transversal multicéntrico en adultos positivos o negativos frente al virus de la inmunodeficiencia humana (VIH) al final de su tratamiento antituberculoso, en consultorios de los estados de Lagos e Ilorin. Todos los pacientes se investigaron mediante la exploración clínica, la radiografía de tórax (CXR), la serología inmunoglobulina G (IgG) para *Aspergillus* y en algunos pacientes el cultivo fúngico de esputo. Se definió la CPA según los siguientes criterios: una serología IgG positiva para *Aspergillus fumigatus* e CXR indicativas o un cultivo positivo para *Aspergillus* de la muestra de esputo con una imagen de aspergiloma en la CXR, presencia de síntomas y enfermedad pulmonar subyacente.

RESULTADOS: Se incluyeron 208 pacientes de junio del 2014 a mayo del 2015. Ciento cincuenta y tres pacientes eran positivos frente al VIH (73,6%). La edad promedio fue 39,8 años, 124 eran mujeres (59,6%) y 39 estaban incapacitados para trabajar (18,8%). En los pacientes aquejados de infección por el VIH con serología IgG positiva para *Aspergillus* la mediana de la cifra de linfocitos CD4 fue 169,5 células/ml (de 4 a 593). Ciento nueve pacientes presentaban TB documentada (52,4%), 140 tos productiva (67,3%) y 50 hemoptisis. La prevalencia de CPA fue 8,7%; en 10 pacientes con infección por el VIH (6,5%) y en ocho pacientes seronegativos frente al virus (14,5%; prueba exacta de Fisher $P = 0,092$).

CONCLUSIÓN: La CPA es una enfermedad desatendida en Nigeria y la mayoría los pacientes cumplen los criterios diagnósticos de TB 'con baciloscopia negativa' de la Organización Mundial de la Salud.