


Primary oral cryptococcosis in an HIV-positive woman with suppressed viral load and normal CD4 count: a rare case

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DESCRIPTION

A 55-year-old HIV-positive woman presented with 16 days of fever, malaise and 10 days of oral mucocutaneous lesions, and a left supraclavicular swelling. She had no history of recent travel, exposure to birds, animals or individuals with tuberculosis. She was married and monogamous with good adherence to the highly active antiretroviral therapy (HAART), atazanavir, ritonavir and emtricitabine/tenofovir. She had a smoking history of 25 pack years of tobacco. Her husband's HIV status was negative. The physical examination revealed normal vital signs except for a body temperature at 38.9°C. The oral examination was significant for a diffused, firm, mildly erythematous and tender mass located in the back of the right inner upper gum and hard palate. There were also lip swelling, oral candidiasis and a greenish purulent secretion in the affected gum (figure 1A). Her neck examination showed a 3×2.5 cm visible and palpable left supraclavicular lymphadenopathy (figure 1B). The rest of the physical examination was normal.

Laboratory studies revealed high levels of C reactive protein (CRP) at 20.30 mg/dL (reference value: 0.0–1.0 mg/dL), erythrocyte sedimentation rate (ESR) at 77 mm/hour (reference value: 0.0–15 mm/hour), alkaline phosphatase (ALP) at 510 U/L (reference value: 40–160 IU/L) and lactic acid dehydrogenase (LDH) at 480 U/L (reference value: 45–90

IU/L). The rest of medical investigation reports are shown in table 1.

A biopsy of the gum and hard palate mass revealed narrow budding fungal bodies with no evidence of malignancy. The papanicolaou stain enhanced the characteristic mucopolysaccharide capsule of the microorganism confirmed as *Cryptococcus neoformans* by Gomori methenamine silver stain (figure 2A–D). The clinical, epidemiological and histopathological findings were consistent with oral cryptococcosis. Fluconazole 400 mg intravenous daily was administered for 2 weeks and continued for 14 weeks orally. The patient experienced complete resolution of fever, oral candidiasis, supraclavicular lymphadenopathy, gum and hard

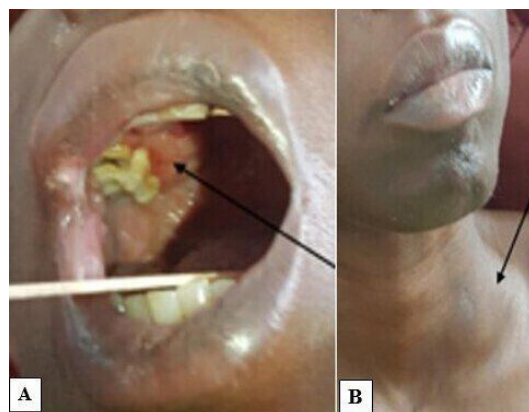


Figure 1 Oral cryptococcosis lesion in a woman living with HIV revealing (A) infiltration of the gum and hard palate (black arrow), lip swelling, oral candidiasis and greenish purulent secretion in the affected gum. (B) Left supraclavicular lymphadenitis (black arrow).

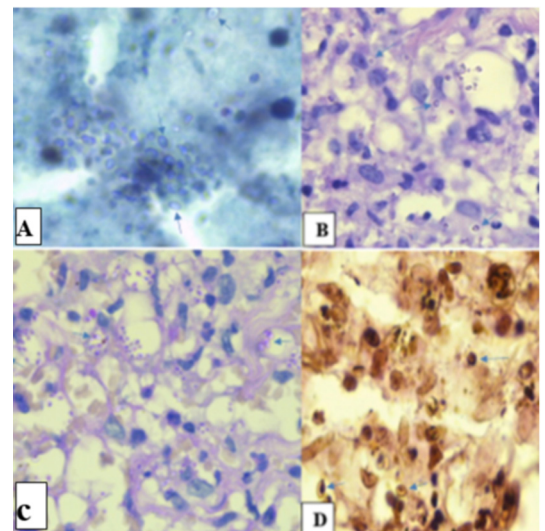


Figure 2 (A–D) Photomicrography of the patient's hard palate lesion showing (A) conventional smear cytology at 40×10 magnification eliciting numerous yeast cells that are pale, slightly refractile spheres ranging from 2 µm to 10 µm in diameter with appearance of asymmetric and narrow-based budding. The papanicolaou stain enhances the characteristic thick mucopolysaccharide capsule of the microorganism. (B) H&E stain at 40×10 magnification shows eosinophilic, uninucleate, spherical, oval and elliptical yeast-like cells surrounded by a wide, clear to faintly stained spherical 'halos' that represent mucinous capsules. (C) Periodic acid-Schiff stain at 40×10 magnification shows round encapsulated budding yeast cells. (D) Gomori methenamine silver stain at 40×10 magnification reveals black staining confirming *Cryptococcus neoformans*.



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Table 1 Medical investigations

Blood test	Result	Reference range
Full blood count, electrolytes, renal and liver function tests	Within normal range	High, low or within normal range
Serum calcium, phosphorous and magnesium	Within normal range	High, low or within normal range
Fasting blood sugar and glycosylated haemoglobin	Within normal range	High, low or within normal range
Hepatitis B and C profile	Negative	Positive, negative, or indeterminate
Venereal disease research laboratory test	Non-reactive	Non-reactive or reactive
Fluorescent <i>Treponema pallidum</i> antibody absorption test	Negative	Positive or negative
Mantoux test, QuantiFERON and PCR test for TB	Negative	Positive or negative
Autoimmune screen: anti-dsDNA, ANF, ANA, Lupus test, Smith antibody	Negative	Negative, borderline, or positive
Vasculitis screen: P-ANCA, C-ANCA	Negative	Negative or positive
Cancer antigens 15-3, 19-9, 125, carcinoembryonic antigen and alpha-fetoprotein tests	Normal	Normal or abnormal
Rheumatoid factor	18 IU/mL	0–20 IU/mL
HIV viral load	42 RNA copies/mL (suppressed)	
CD4+ T-cell count	452 cells/μL. Normal	410–1590 cells/μL
Human T-cell leukaemia-lymphoma virus I and II antibodies	Negative	Negative or positive
Other tests	Result	Reference range
ECG, echocardiogram	Normal	Normal or abnormal
Chest X-ray	Normal	Normal or abnormal

ANA, antinuclear antibody; ANF, antinuclear factor; anti-dsDNA, antidouble-stranded deoxyribonucleic acid; C-ANCA, cytoplasmic antineutrophil cytoplasmic antibody; P-ANCA, perinuclear antineutrophil cytoplasmic antibodies; TB, tuberculosis.

palate lesion, and normalisation of CRP, ESR, ALP and LDH over 2 weeks and is receiving outpatient follow-up and further care.

Oral and mucocutaneous cryptococcal infections have rarely been documented in the literature. A review of the literature revealed seven cases of cryptococcal infection with oral manifestations prior to 2016: five of them occurred in HIV positive and/or patients with AIDS, one in an immunosuppressed stem cell transplant recipient, and one in an immunocompetent host. The lesions were located in the palate (two cases), tongue (two cases), maxilla (one case), mandibula (one case) and salivary glands (one case).¹

Cryptococcal infection can affect the lungs and almost any other organ. However, on dissemination, the fungus has an especial tropism for the central nervous system, frequently causing meningitis.^{1–3} Cryptococcal meningitis occurs when the CD4 count decline below 100 cells/mm³. In 2006, over a million cases

of cryptococcal meningitis were reported worldwide.² Systemic cryptococcosis currently kills over half a million individuals annually, mainly in Africa.²

Our patient is currently well controlled on HAART with an undetectable HIV viral load and a CD4 count greater than 400. To the best of our knowledge, oral cryptococcosis in an HIV-positive woman with suppressed viral load and CD4 count greater than 400 is a rare manifestation. This is probably the first case being reported.

Learning points

- ▶ *Cryptococcus neoformans* is a ubiquitous yeast discovered in 1894 by Abraham Buschke and Otto Busse who isolated it from a lesion located in the tibia of a woman.
- ▶ Oral cryptococcosis is a mycosis of the oral cavity that has rarely been reported except in patients with HIV, where the use of highly active antiretroviral therapy and fluconazole can prevent and treat most cases.
- ▶ Chronic, bizarre oral or maxillary pathology should indicate a systemic mycosis work up because of the risk for systemic cryptococcosis and meningitis which kills over half a million individuals annually, mainly in Africa.

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REFERENCES

- 1 DiNardo AR, Schmidt D, Mitchell A, *et al.* First Description of Oral *Cryptococcus neoformans* Causing Osteomyelitis of the Mandible, Manubrium and Third Rib with Associated Soft Tissue Abscesses in an Immunocompetent Host. *Clin Microbiol Case Rep* 2015;1:017.
- 2 Park BJ, Wannemuehler KA, Marston BJ, *et al.* Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. *AIDS* 2009;23:525–30.
- 3 Srikanta D, Santiago-Tirado FH, Doering TL. *Cryptococcus neoformans*: historical curiosity to modern pathogen. *Yeast* 2014;31:47–60.

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