CASE REPORT

Disseminated cryptococcosis involving the head and neck

Matthew Lazzara, Arjun Joshi

The George Washington University, Washington, DC, USA

Correspondence to

Dr Arjun Joshi,
ajoshi@mfa.gwu.edu

SUMMARY

A middle-aged patient with HIV presented with very distinctive maculopapular cutaneous lesions involving the face and lymphadenopathy confined to the neck. A diagnosis of disseminated cryptococcosis was made based on pathological analysis of lymph node and skin lesions.

BACKGROUND

The incidence of AIDS in certain areas of the world continues to increase, despite novel anti-retroviral therapies and better access to healthcare. It is imperative for the treating otolaryngologist to understand the common manifestations of rare conditions in the immunocompromised state—whether it be from diabetes, transplantation or acquired immunodeficiency—in order to avoid any treatment delays. Immunocompromised patients can have rapid progression of seemingly benign infectious disease, and short delays in diagnosis can have catastrophic consequences.

CASE PRESENTATION

A middle-aged patient presented to the hospital with cutaneous facial lesions over the course of several months. The patient's medical history was significant for HIV of 20 years duration, and the recent CD4 count was 4. There was a positive history for intravenous drug use.

At presentation, the patient's temperature was 103°F, heart rate was 124 and blood pressure was 111/58. Physical examination was notable for multiple tender maculopapular cutaneous lesions involving the face and neck (figure 1). In addition, there was diffuse bilateral cervical adenopathy with tender, mobile lymph nodes, some measuring up to 3.5 cm. There were no focal neurological signs and no signs of meningismus.

INVESTIGATIONS

A CT of the neck with contrast was performed which revealed numerous diffuse hypodense rim-enhancing lymph nodes, with similar lesions seen within the parotid glands bilaterally (figure 2).

A chest X-ray was performed which demonstrated a diffuse interstitial infiltrate.

Initial blood cultures were negative. A complete blood count was performed and was negative for bandaemia or leukocytosis.

A sputum culture was negative for any organisms.

Fine-needle aspiration biopsy was inconclusive and suggestive of polymorphous lymphocytes consistent with a reactive process.

An open cervical nodal biopsy as well as a punch biopsy of a skin lesion was performed. Microscopic examination demonstrated partial destruction of nodal architecture without a significant inflammatory response. There were numerous spherical, narrow-based budding, encapsulated yeast (figure 3). The capsules and walls stained positive with Gomori methenamine silver (GMS; figure 4). A diagnosis of cutaneous cryptococcosis was then made.

Lumbar puncture was then performed after the diagnosis of cutaneous cryptococcosis, in order to rule out disseminated cryptococcosis, given the predilection for central nervous system (CNS) involvement. Lumbar puncture was negative for organisms, demonstrated a normal cerebrospinal fluid analysis pattern, cryptococcal antigen (CrAg). Serum CrAg was also then checked and found to be markedly positive at 1024. A diagnosis of disseminated cryptococcosis was then made.

DIFFERENTIAL DIAGNOSIS

Evaluation of neck masses arising in patients with HIV infection should include parotid pathology (benign lymphoepithelial cyst), other infectious processes (*Mycobacterium avium* complex, histoplasmosis, coccidioidomycosis) and various

Figure 1 Characteristic cutaneous lesions.

CrossMark

To cite: Lazzara M, Joshi A. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202306

Figure 2 CT of the neck with contrast demonstrating numerous diffuse hypodense rim-enhancing lymph nodes, with similar lesions seen within the parotid glands bilaterally.

neoplasms (Kaposi's sarcoma, non-Hodgkin's Lymphoma).^{1 2} Benign generalised lymphadenopathy should be diagnosed after excluding all pertinent diseases.

The diagnosis of disseminated cryptococcosis was confirmed only after measurement of serum CrAg. The diagnosis of cutaneous cryptococcosis was suggested by the patient's severe immunodeficient state, longstanding problems of fever, fatigue and headache and the suspicious skin lesions.

TREATMENT

Therapeutic options are typically guided by immune status and extent of disease. For those patients with significant disease, initial therapy usually includes amphotericin B with or without the addition of flucytosine and fluconazole.³ Initiation or resumption of highly active antiretroviral therapy (HAART) in the presence of AIDS-defining disease is essential to successful long-term therapy, and life-long maintenance with fluconazole is usually indicated. After starting antiretroviral therapy, patients may develop signs and symptoms of an acute cryptococcal meningitis or lymphadenitis secondary to the return of inflammatory mediators. This phenomenon is known as the immune reconstitution syndrome.⁴

Figure 3 Numerous spherical, narrow-based budding, encapsulated yeast.

Because of our patient's delicate immune status and the dissemination of infection, intravenous amphotericin B and flucytosine were started for a total of 4 weeks until blood serum titres demonstrated a threefold dilution and were considered appropriate.

OUTCOME AND FOLLOW-UP

The patient was unfortunately lost to follow-up after completing intravenous amphotericin B and flucytosine. Despite many attempts, we have not been able to reconnect to establish care.

DISCUSSION

Cryptococcosis is caused almost exclusively by the species *Cryptococcus neoformans*, a ubiquitous fungal organism which is found in soil and bird excreta throughout the world. The introduction of HAART has resulted in a significant decline in the incidence of this disease entity, as well as other AIDS-defining diseases. Nonetheless, mortality rates associated with cryptococcosis have not changed significantly, especially in those patients without access to adequate healthcare. Other immunocompromised populations are also affected—comorbidities such as diabetes, cancer, lung disease and rheumatological/immunological diseases place the affected people at higher risk for morbidity and mortality.¹ The Center for Disease Control estimates that there are 0.4–1.3 cases of cryptococcosis/100 000 in the general US population, with a mortality rate of 12%.

Cryptococcosis is the most common life-threatening mycosis associated with AIDS worldwide and develops in approximately 2–5% of immunocompromised patients per year in the USA.² Exposure usually occurs through inhalation of aerosolised propagules. In the alveoli of normal, healthy individuals, they are quickly phagocytosed by macrophages, and are either destroyed or sequestered in granulomas. Poor cell-mediated immunity appears to be the primary problem predisposing to widespread dissemination. *C. neoformans* has been isolated from virtually every tissue type, including the skin, spleen, liver, kidney, prostate, heart, bone and eyes. Specifically in the head and neck, it has shown to involve the nasopharynx, paranasal sinuses, tonsils, oral cavity and larynx.⁵

Clinically, however, the disease has a predilection for the lung, and especially, the CNS. CNS manifestations commonly include headache, fever, cranial nerve palsies, lethargy, coma or memory loss over several weeks. While the severity of respiratory tract symptoms can vary, lung findings can include nodules,

Figure 4 Positive staining of capsules and walls with Gomori methenamine silver.

Learning points

- ▶ There are multiple different aetiologies of neck masses in individuals who are HIV positive and include neoplasm, infection and inflammatory pathologies.
- ▶ Fine-needle aspiration is considered the first-line test for a neck mass in a patient who is HIV positive, but usually a definitive diagnosis is made on excisional nodal biopsy.
- ▶ Generalised lymphadenopathy and characteristic cutaneous lesions in HIV, as seen in this report, would provide clue to the clinician in the diagnosis of disseminated cryptococcosis.
- ▶ Cutaneous cryptococcosis usually precedes the onset of more serious disseminated cryptococcosis, and should be readily diagnosed in order to prevent serious consequences.
- ▶ Lumbar puncture and cerebrospinal fluid analysis as well as serum analysis should be performed for diagnosing disseminated or central nervous system disease, and treatment is usually guided by either serum or cerebrospinal fluid antigen titres.

lobar and interstitial infiltrates, hilar lymphadenopathy, effusions and cavitations.

Skin involvement can range from a small papule to severe cellulitis or abscess-like lesions mimicking bacterial infections.⁵ Cryptococcosis can present as cervical lymphadenitis in HIV-positive patients, although it is far less common than tuberculosis or benign reactive adenopathy.⁶ Less than 12 cases have been described in the literature.⁵ Most often the manifestation of cutaneous cryptococcosis precedes the onset of more serious systemic or disseminated cryptococcosis by 1–2 weeks.

Routine diagnosis is made by microbiological culture, histopathological examination or serology. Pulmonary nodules should be worked-up with sputum and possibly bronchoscopic examination, and blood cultures and cerebrospinal fluid should be analysed to determine dissemination. Fine-needle aspiration

is often employed in the evaluation of neck masses of unknown aetiology. Because of the significant possibility of lymphoma in these cases, an open biopsy can also be performed.

Under microscopic examination of tissue samples or cultures, one can classically identify budding fungi which stain with India ink (specific for fluids) or GMS stain. Serological tests are most often used, especially in cases of CNS involvement. Latex agglutination and enzyme immunoassay tests for serum antigen are highly sensitive and specific (>90%).⁴ HIV-positive patients with cryptococcosis have higher rates of CNS and extrapulmonary infections, more positive blood cultures and higher polysaccharide antigen titres when compared with non-HIV infected individuals.⁷

AIDS-defining diseases have been shown to manifest in the head and neck in nearly all cases.² It is up to the otolaryngologist to assist and promptly diagnose these conditions, as a delay in diagnosis can result in unnecessary morbidity and potential mortality.

Contributors AJ and ML were responsible for the idea for the case report, the research and drafting the report along with the final revisions.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Barzan L, Tavio M, Tirelli U, *et al.* Head and neck manifestations during HIV infection. *J Laryngol Otol* 1993;107:133–6.
- 2 Lee KC, Cheung SW. Evaluation of the neck mass in human immunodeficiency virus-infected patients. *Otolaryngol Clin North Am* 1992;25:1287–305.
- 3 Saag MS, Graybill RJ, Larsen RA, *et al.* Practice guidelines for the management of cryptococcal disease. *Clin Infect Dis* 2000;30:710–18.
- 4 Woods ML, MacGinley R, Eisen DP, *et al.* HIV combination therapy: partial immune restitution unmasking latent cryptococcal infection. *AIDS* 1998;12:1491–4.
- 5 Mandell G, Bennett J, Dolin R. Principles and practice of infectious diseases. New York: Churchill Livingstone Inc, 2005:2997–3012.
- 6 Garbaly RS, Basu D, Roy S, *et al.* Cryptococcal lymphadenitis: report of a case with fine needle aspiration cytology. *Acta Cytol* 2005;49:58–60.
- 7 Shoham S, Levitz SM. The immune response to fungal infections. *Br J Haematol* 2005;129:569–82.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow