A mistaken diagnosis of *Molluscum contagiosum* in a HIV-positive patient in rural South Africa

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SUMMARY

A 25-year-old gentleman presented with multiple small ulcerations and papules covering a large portion of his face and neck, associated with general malaise. He was HIV seropositive with a total CD4 count of 78 cells/ μ l. A diagnosis of *Molluscum contagiosum* was made and the patient discharged. He re-presented 3 weeks later with a 2-day history of progressively worsening headache associated with photophobia and diarrhoea. The generalised skin eruption had worsened, now involving his torso and upper limbs. Cerebrospinal fluid examination was highly positive for cryptococcal antigens and the patient was started on amphotericin B. Skin biopsy confirmed cutaneous *Cryptococcus neoformans*. After 4 days, the headache and photophobia resolved. A mild improvement in his skin was seen after completing 14 days of treatment. He was discharged with lifelong fluconazole therapy.

BACKGROUND

Cryptococcal meningitis is extremely common in areas with a high prevalence of HIV. It is now reported as the most common cause of meningitis in Southern Africa.¹ It has been associated with a mortality rate of up to 20%,² hence early diagnosis and treatment is essential to ensure a favourable outcome. The usual presentation is headache, fever, nausea and vomiting, neck stiffness, abnormal behaviour and photophobia. However, ulcerating skin lesions are also a recognised sign of disseminated cryptococcal disease.

We present a case where a diagnosis of cryptococcosis was delayed because of failure to recognise cutaneous signs of the disease. Although *Molluscum contagiosum* is prevalent in the Southern African population, it is distinguishable from cryptococcal lesions by its lack of ulceration. It highlights the importance of a full history and examination and the importance of adequate investigation of skin lesions in severely immunocompromised patients, especially when associated with systemic symptoms.

CASE PRESENTATION

A 25-year-old gentleman presented to casualty complaining of new onset skin lesions on his face and neck that started a week ago (figure 1). This was associated with loss of energy and nausea. He was HIV seropositive, having been recently diagnosed at his local clinic. He was unaware of his CD4 count, but was in the process of antiretroviral therapy initiation. There was no other significant medical history, and he was on no regular medications.

On examination he had no fever with a regular pulse rate of 80 beats/min, blood pressure of 115/62 mm Hg and a respiratory rate of 16/min.

Glasgow Coma Score (GCS) was 15/15. Multiple small ulcerations and papules with central umbilication were noted, covering a large portion of his face and neck. It spread across several dermatomes and followed no particular pattern. They were of different sizes, ranging from 5 mm to 3 cm in diameter, and were all non-tender and non-pruritic. The rest of the examination was non-remarkable. A spot diagnosis of *M. contagiosum* was made and the patient was sent home to be followed up by his local clinic.

He re-presented 3 weeks later to the casualty department, now complaining of a 2-day history of worsening headache associated with photophobia, diarrhoea and general malaise. The skin eruption had spread to his torso and upper limbs. On examination, he remained afebrile with a regular pulse rate of 110 beats/min, blood pressure of 125/68 mm Hg and a respiratory rate of 16/min. GCS was 15/15. Again, the lesions consisted of non-tender ulcerations and papules and many had small bleeding points. The chest was clear to auscultation, and the abdomen was soft and non-tender. There were no focal neurological signs.

INVESTIGATIONS

Routine bloods showed a neutrophilia of $12.3 \times 10^3/\text{mm}^3$ and a positive C reactive protein. CD4 count was 78 cells/ μ l.

Chest radiograph was normal.

Lumbar puncture was performed, given the history of headache, photophobia and immunodeficiency. Analysis of the cerebrospinal fluid (CSF) yielded the following results: polymorphs 0 (normal), lymphocytes 32 (raised), protein 1.2 (raised) and glucose 3.1 (normal). Rapid cryptococcal antigen test was positive. Encapsulated yeast cells were observed on India Ink stain. There was no growth on the CSF culture. CSF opening pressure was normal.

A skin punch biopsy confirmed infection with the fungal species, *Cryptococcus neoformans*.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for skin manifestations of cryptococcosis include

- ▶ *M. contagiosum*
- ▶ Basal cell carcinoma
- ▶ Keratoacanthoma
- ▶ *Histoplasma capsulatum*
- ▶ *Coccidioides immitis*
- ▶ *Penicillium marneffei*
- ▶ Herpes Zoster

TREATMENT

The diagnosis of disseminated cryptococcal meningitis was explained to the patient, and the initial

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treatment phase consisted of a course of intravenous amphotericin B (1 mg/kg daily). Adjuvant corticosteroid therapy was also administered in the form of intravenous dexamethasone for 5 days. Throughout the course of treatment, renal function was monitored. The patient completed the 14 day course with no documented adverse effects and renal function remained normal. He was then switched to a consolidation phase of treatment, consisting of a 4-week course of fluconazole (400 mg daily). At this point, the patient was initiated on antiretroviral therapy.

OUTCOME AND FOLLOW UP

The patient's symptoms of headache, photophobia and nausea resolved after day 3 of amphotericin, and did not require therapeutic CSF pressure management. The skin lesions improved significantly after completing the course of intravenous treatment. On discharge, the patient was followed up in his local clinic to continue lifelong fluconazole therapy.

DISCUSSION

HIV-associated cryptococcosis is a spectrum of diseases commonly caused by the encapsulated yeast *C neoformans*, and affects severely immunocompromised individuals (CD4 < 200 cells/ μ l). It usually presents as a sub-acute meningo-encephalitis, with symptoms of headache, photophobia, neck stiffness, abnormal behaviour, malaise, nausea and vomiting and diarrhoea. Cutaneous dissemination occurs in approximately 5% of cases, and can often precede systemic symptoms of the disease. This has a characteristic appearance of umbilicated ulcerating papules with bleeding points, and is often associated with general malaise and mild fever.³

M contagiosum is also very common in HIV seropositive patients, and presents as small, discrete shiny lesions with central umbilication.⁴ Unlike cutaneous cryptococcosis, these do not ulcerate or bleed (figure 1).

Diagnosis is usually achieved via CSF analysis, which can be conducted promptly in most hospital settings in South Africa. Lumbar puncture should therefore be attempted in all immunocompromised patients who present with the above symptoms, assuming that there are no focal neurological signs. The presence of characteristic skin lesions in an unwell patient also warrants immediate investigation via a lumbar puncture to prevent dangerous delay in diagnosis. CSF is sent for cryptococcal antigen detection and India Ink stain, in addition to cell count, chemistry and culture. A CT head is mandatory prior to lumbar puncture in the presence of focal neurological signs.

Figure 1 The small mass on the upper lip may initially be mistaken for *Molluscum contagiosum*, however it will soon ulcerate and become similar in appearance to the lesions seen on the patient's eyebrow and forehead.

Treatment consists of antifungal therapy. The use of amphotericin B has been associated with better outcomes than fluconazole in resource-poor settings. A test dose is given beforehand, and the patient is observed for signs of anaphylaxis. If there are no adverse effects, amphotericin B is continued for 14 days. Monitoring of renal function throughout this treatment is essential due to nephrotoxic effects of the drug. If there are serious adverse effects or deterioration in renal function, amphotericin B is usually stopped and high-dose fluconazole is used instead. Lifelong low-dose fluconazole is recommended for immunocompromised patients to prevent recurrence of the disease.⁵

Cryptococcal disease is associated with a high mortality rate in patients with HIV, thus prompt diagnosis and treatment is essential. Although cutaneous manifestations of the disease are not common, it may precede the development of serious systemic symptoms of disseminated disease, as demonstrated in this case. Most institutions in South Africa have facilities to allow for a skin biopsy, and this should be utilised in suspected cases of cutaneous involvement. In a rural setting, specimens are sent to regional centres for analysis so it may take up to 2 weeks to obtain results from such a biopsy. However, this should not be a deterrent.

Learning points

- ▶ Cryptococcosis may present with cutaneous lesions, which can precede the onset of systemic symptoms of meningo-encephalitis in the HIV-positive patient.
- ▶ Recognition of characteristic skin lesions can aid early diagnosis of potentially fatal disseminated cryptococcal disease, and improve outcomes.
- ▶ One should have a high index of suspicion for cryptococcal disease when faced with an unwell severely immunocompromised patient.
- ▶ The facility to perform skin biopsies is readily available in most institutions in South Africa, and should be considered in any unwell HIV-positive patient presenting with new or changing skin conditions.

Competing interests None.

Patient consent Obtained.

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