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Case Report Open Access

Concomitant and Disseminated Infections due to Non-typhi *Salmonella* and *Cryptococcus neoformans* in AIDS Patients. Report of 2 Cases and Review of the Literature

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Introduction

Opportunistic infections (OI) are an important and frequent cause of morbidity and mortality in patients with acquired immunodeficiency syndrome (AIDS), especially in those who not receiving highly active antiretroviral therapy (HAART) or those who unknown their serological status to the retrovirus and finally, those who have a poor adherence to antiretroviral therapy.

Infection with non-typhoid *Salmonella*, typically causes enteritis in healthy individuals, but can lead to severe septicemia in immunocompromised hosts, especially those patients with HIV/AIDS disease [1]. In addition to septicemia, atypical infections as osteomyelitis, empyema, pulmonary abscesses, pyelonephritis or meningitis have been described [2].

Recurrent episodes are characteristic of non-typhoidal *Salmonella* septicemia in the AIDS population and are mainly associated with *Salmonella enterica* serotype *Enteritidis* or *Salmonella enterica* serotype *Typhimurium*. Since 1987, recurrent nontyphoidal *Salmonella bacteremia* has been included as an AIDS-defining illness. In the pre-HAART era, up to 45% of persons with HIV infection will have recurrent bacteremia due to *Salmonella* but the incidence decreased significantly in the HAART era [3].

Cryptococcosis is a fungal illness with high mortality rate and represents the second most common infection of the central nervous system (CNS) in patients with AIDS. In immunocompromised patients, particularly those with AIDS, meningoencephalitis is present in more than 90% of cases, generally in the context of disseminated cryptococcal disease [4].

Here, we present two cases of non-typhi *Salmonella bacteremia* complicated with abscesses and cryptococcal disseminated infection occurring in females with advanced HIV/AIDS disease.

Case Reports

Case 1:

A 38-year-old female, infected with the human immunodeficiency virus (HIV), was admitted to our unit of AIDS-related illness with fever, headache, diffuse and colicky abdominal pain and right knee pain. Relevant physical examination findings include fever (38.5°C), spontaneous epigastric and right flank abdominal pain, increased during palpation but without signs of peritoneal irritation. Examination of right knee showed signs of acute septic arthritis (severe pain that worsens with the movements, swelling, warmth and redness over the joint). Initial relevant laboratory findings were red blood cells (RBC) 4.65×10^{12}, haemoglobin 12.4 gm, white blood cell (WBC) count of 3.4×10^{12}, platelets 274×10^{9}. Liver and renal function was normal and lactate dehydrogenase level was 409 U/l. The CD4 T cell-count was 34 cell/µl; antiHCV and HBV antibodies were negatives. Blood cultures were positive for non-tiphy *Salmonella*. An echocardiography showed no pathological alterations. A lumbar puncture revealed the presence of capsulated yeasts with a double refractive wall compatible with Cryptococcus. Cerebral spinal fluid (CSF) culture showed colonies of *Cryptococcus neoformans*, identified as *C. neoformans* var neoformans.

Abdominal ultrasound revealed a large and heterogeneous image of 75 mm × 33 mm on the right flank, surrounding the aorta and lymph nodes, with irregular contours and hypoechoic areas compatible with abscess (Figures 1, 2 and 3).

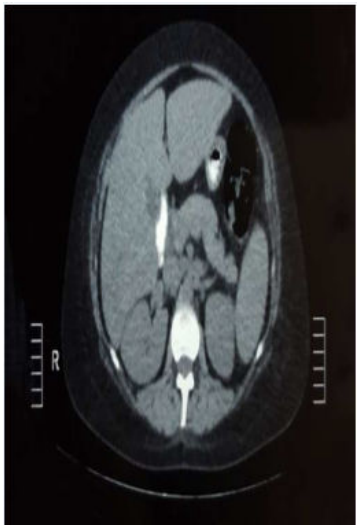

Figure 1: Computed tomography abdominal scan with water density oral and intravenous contrast corresponding to patient one showing a large and heterogeneous intra-abdominal collection.

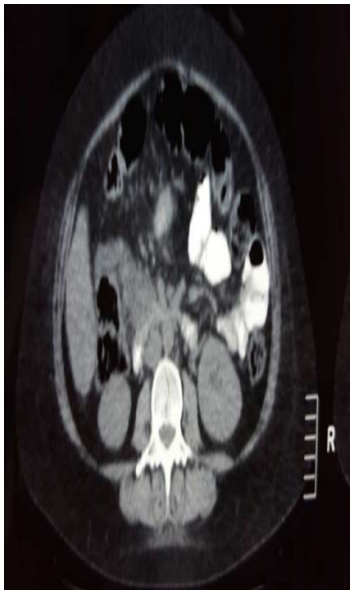

Figure 2: Computed tomography abdominal scan with oral and intravenous contrast of the one patient: large, relatively well-circumscribed heterogeneous collection in the abdominal cavity surrounding the aorta and lymph nodes, some of them with heterogeneous enhancement.

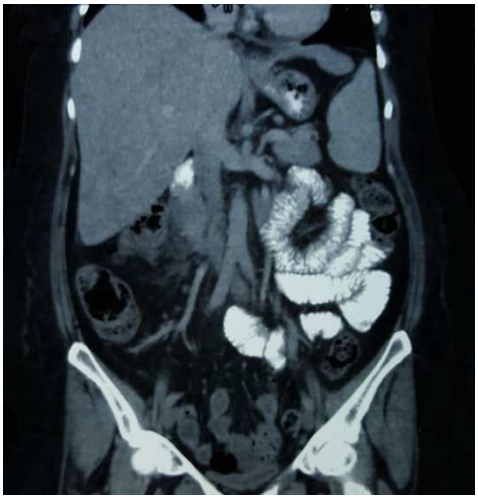

Figure 3: Computed tomography abdominal scan with oral and intravenous contrast: a large intra-abdominal, intraperitoneal, pus collection (abscess) that extending since the upper abdominal almost the pelvic cavity.

An articular ultrasound of the right knee showed increased intra-articular fluid compatible with septic arthritis. An arthrocentesis of the right knee was performed to take a sample of synovial fluid; it was sent to the identification of common bacteria, mycobacteria and fungi. Bacteriological direct examination showed Gram negative bacilli that in culture were characterized as Non-tiphy *Salmonella*. Initially, she was treated with intravenous ciprofloxacin at doses of 400 mg/daily with a partial response. An exploratory laparotomy was performed; a large intra-abdominal abscess was palpable. A surgical drainage was made and abundant purulent material was obtained. Direct examination and culture revealed Non-tiphy *Salmonella*.

Non-tiphy *Salmonella* identified in blood cultures, articular fluid and intra-abdominal abscess was sensitive to cefotaxime, ampicillin, ciprofloxacin, imipenem and trimethoprim-sulfametoxazol. Meropenem was added to the antimicrobial scheme.

After one month of treatment, the patient was discharge in a good clinical condition.

Case 2

A 43-year-old female, HIV seropositive and with diagnosis of AIDS since two years before, due to diagnosis of Kaposi's sarcoma of oral mucosae, was admitted for fever, headache, weight loss, night sweats, chills, symptoms of urinary tract infection (upper back and side pain, frequent and painful urination) with episodes of bacteremia. Initial relevant laboratory findings include RBC 2.89×10^{12} cell/l, hematocrit 30%, WBC 4.2×10^{9} cell/l (79% neutrophils and 12% lymphocytes), platelets 257×10^{9} l. Liver and renal function was normal. The CD4 T-cell count was 22 cell/µl and the plasma viral load was 188 900 copies/mL (log10 5.28). Anti HVB and HCV antibodies were negatives. A lumbar puncture was performed and revealed *Cryptococcus neoformans* infection in the India ink direct examination and culture. Cerebral computed tomography (CT) scan showed only moderate central atrophy. Initial blood and urine cultures showed of Non-tiphy *Salmonella* susceptible to ceftriaxone and ciprofloxacin. Abdominal ultrasound revealed hepatomegaly, splenomegaly with multiple hypoechoic lesions and mild increased parenchymal echogenicity in the kidneys. A thorax computed tomography scan showed and homogeneous opacity in the right lower lobe with a mild pleural effusion.

Diagnosis of pyelonephritis with bacteremia (urosepsis) due to Non-tiphy *Salmonella* and disseminated cryptococcosis with central nervous system involvement was made. Based on these two confirmed diagnosis therapy with ciprofloxacin, amphotericin B and fluconazole was initiated.

Patient presented a good clinical evolution and treatment response and was discharged after 3 weeks of treatment.

Discussion

Bacteremia due to Non-tiphy *Salmonella* is a frequent complication in HIV-infected patients, especially in those who did not receive HAART or present a poor adherence and is generally associated with a poor prognosis. In this kind of patients, bacteremia is responsible for the immediate cause of death in up to 32% of patients, especially in intravenous drug abuse, use of a central venous catheter (CVC), and those with neutropenia and a low CD4 T-cell count [5]. Previous studies demonstrated a variable distribution of organisms causing bacteremia in AIDS patients. The most common pathogens described have been *Staphylococcus aureus*, *Streptococcus pneumoniae* and, especially, *Salmonella* spp [6,7].

Salmonella bacteremia is one manifestation of severe immunosuppression in patients with HIV infection, and the development of bacteremia represents a frequent and severe complication in AIDS patients. Persons with HIV infection have an estimated 20- to 100-fold increased risk of salmonellosis compared

with the general population [8]. Recurring, non-typhoid *Salmonella* septicemia is considered an AIDS-defining illness. The risk of recurrent septicemia decreased significantly in the HAART era [9].

Despite the frequency of *Salmonella bacteremia* in HIV-infected patients, focal or suppurative infections have been rarely described. Single case reports of renal, lungs, bones and joints, vascular system, CNS, abdominal cavity, and soft tissue abscesses have been published [10]. *Salmonella* is more likely to cause severe invasive disease in persons with acquired immunodeficiency syndrome (AIDS) than in immunocompetent persons [11].

The incidence of neurocryptococcosis in AIDS patients is strongly related with a low level of CD4 T-cell counts, as we can see in these patients [12]. Meningoencephalitis due to *Cryptococcus neoformans* is the third most common intracranial infection in AIDS patients, including 70% to 90% of all the cases, only surpasses by the own retrovirus HIV and the *Toxoplasma gondii* encephalitis. CNS involvement is secondary to the haematogenous spread, usually from a reactivation of a prior pulmonary infection. The basal meninges of the brain are especially affected; meningeal infection may involve the brain parenchyma or may extend along the Virchow-Robin spaces at the level of the thalams, basal ganglia, periventricular white matter and the cerebellum. Neuroimages can show the leptomeningeal enhancement and small lesions can be seen in the cerebral periventricular white matter named as gelatinous pseudocysts. Also, with less frequency, a large size lesions named as cryptococcomas can be observed in the brain tissue [13]. AIDS patients with cryptococcal meningitis differ from non-HIV-infected subjects in that they present a little inflammatory response in CSF, large fungal burden and a less frequency of mass lesions [14].

Concomitant and unusual opportunistic infections are a frequent clinical finding in patients with HIV infection and a low CD4 T-cell count. It is also important to understand this possibility to indicate a correct and complete antimicrobial treatment.

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