Disseminated *Mycobacterium Simiae* with Pelvic Malakoplakia in an AIDS Patient

Maria Nina Chitasombat[1] and Duangkamon Wattanatranon[2]

[1]Division of Infectious Disease, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.
[2]Division of Anatomical Pathology, Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

ABSTRACT: Malakoplakia in an acquired immunodeficiency syndrome (AIDS) patient with disseminated *Mycobacterium simiae* infection presented with a large pelvic mass that caused organ dysfunction from mimicking a tumor. Malakoplakia is a rare, chronic granulomatous abnormal host response toward infectious agents, presenting as a tumor-like lesion. This is the first report of pelvic malakoplakia after disseminated *M. simiae* infection in an AIDS patient.

KEYWORDS: malakoplakia, *Mycobacterium simiae*, AIDS

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CORRESPONDENCE: mchitasombat@gmail.com

Case Report

A woman in her 30s with acquired immunodeficiency syndrome (AIDS) diagnosed by the fourth-generation HIV testing, with a CD4 count of 3 (1%) cells/mm^3, presented with weight loss and cachexia. She was started on lamivudine, zidovudine, and nevirapine and then developed hypersensitivity rash and hepatitis. At that time, she also had pancytopenia (white blood cells 2,950/μL, neutrophils 79%, lymphocytes 13%, hemoglobin 9.6 g/dL, hematocrit 29%, platelets 325,000 × 10^9/L) and intra-abdominal lymphadenopathy. Bone marrow study showed poorly formed granuloma. She was treated initially for presumptive disseminated mycobacterial infection with isoniazid, rifampicin, pyrazinamide, ethambutol, and clarithromycin. She improved clinically, and her antiretroviral regimen was restarted after three weeks with lamivudine, tenofovir, and efavirenz. Later on, she had gained weight, and laboratory results showed the resolution of pancytopenia and hepatitis. Bone marrow culture grew *Mycobacterium simiae*, which was identified by molecular sequencing technique. Her antimicrobial regimen was changed to clarithromycin, ethambutol, and ciprofloxacin. Two months later, the antibiotic regimen was readjusted to ciprofloxacin, clarithromycin, and streptomycin injection (for one month) according to the susceptibility, and her clinical improvement was remarkable. Two months after the initiation of antiretroviral therapy (ART), she had an HIV viral load of <40 copies/mL and a CD4 count of 1 (2%) cell/mm^3; however, she had recurrent transaminitis. She was given prednisolone 20 mg/day with a tapered dose for five weeks for the treatment of hepatitis possibly due to immune reconstitution inflammatory syndrome. Five months after the initiation of ART, her CD4 count was 13 (3%) cells/mm^3, with an HIV viral load of <40 copies/mL. She developed cytomegalovirus retinitis and received intravitreal ganciclovir injection and oral valganciclovir for six weeks. She then developed abdominal pain, with a palpable large suprapubic mass, for three weeks. She had no dysuria or vaginal discharge prior to the onset of abdominal pain. A pelvic examination showed no cervical discharge, and urinalysis was normal. A computed tomography (CT) scan of the abdomen showed a large lobulated mass (8.5 × 10 cm) with the epicenter at the right adnexa and with the invasion of the uterus, right ovary, right lateral wall of the sigmoid colon, appendix, superior wall of the urinary bladder, and right distal ureter, causing right ureter obstruction and a moderate degree of right hydronephrosis. Multiple matted lymph nodes were present along the mesenteric root and in the para-aortic, aortocaval, and retrocaval regions. Focal circumferential wall thickening of the left side of the jejunum caused moderate intraluminal narrowing, with evidence of small bowel obstruction (Fig. 1). She underwent exploratory laparotomy; intraoperative findings revealed a large pelvic mass with nodular surface and with dense adhesion to the omentum, the anterolateral wall of the uterus, the bladder, and the sigmoid colon. Only partial resection of the omentum and a biopsy of the mass at the anterior aspect of the uterus were performed. Pathologic examination revealed malakoplakia (Fig. 2). Acid-fast and Gomori methenamine stains of the tissue specimen were negative; however, microbial culture

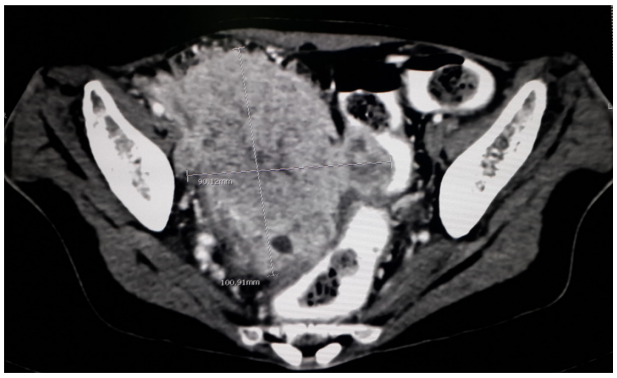

Figure 1. CT scan of the abdomen showing a large pelvic mass compressing the urinary bladder.

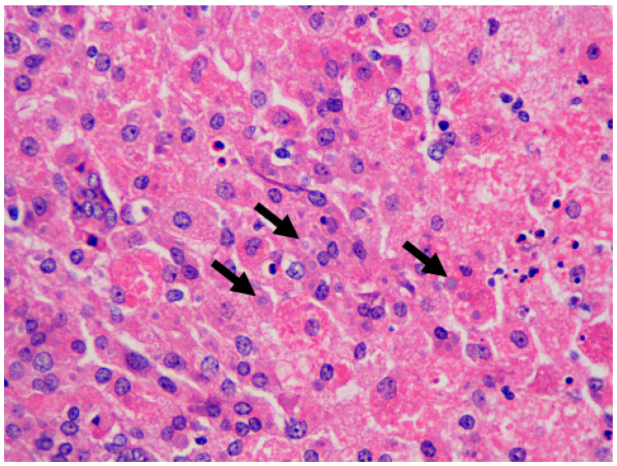

Figure 2. High-power photomicrograph (400× , hematoxylin and eosin stain) of the pelvic mass revealed the aggregations of histiocytes with granular eosinophilic cytoplasm (von Hansemann histiocytes), many of which contained basophilic inclusions (Michaelis–Gutmann bodies) (arrows), typically spherical, 5–8 µm, and concentrically laminated bodies with a bull's-eye appearance.

was not sent for laboratory analysis. Her hospital course was complicated by wound infection/dehiscence, with the formation of an enterocutaneous fistula. She was treated with intravenous antibiotics and total parenteral nutrition therapy. She suffered from abdominal pain as well as malnutrition due to the nature of the unresectable residual mass and the enterocutaneous fistula. She was discharged home on palliative care, with antimicrobial therapy, and was lost to follow-up.

Disseminated *M. simiae* infection presented with pancytopenia, hepatitis, and lymphadenopathy, similar to *Mycobacterium avium* infection in an AIDS patient.[1] Effective antimicrobial treatment of *M. simiae* included rifampicin and ciprofloxacin. Our patient had an abnormal host immune response to infection, malakoplakia, which occurred after *M. simiae* infection, a condition that has not been previously described in the literature. However, we were unable to demonstrate a direct correlation due to the lack of microbiological data from tissue specimens.

Malakoplakia has a gross appearance of round, oval, or mushroom-shaped yellowish structures.[2] Histologically, there is a proliferation of histiocytes with abundant granular eosinophilic cytoplasm (known as von Hansemann histiocytes) that contain the pathognomonic Michaelis–Gutmann bodies.[2] These bodies are round to oval in shape and are visible as deeply basophilic structures, which are typically described as target-like and are periodic acid–Schiff stain-positive and calcium-positive.[2] Pathogenesis of malakoplakia is associated with the lysosomal dysfunction of macrophages in the intracellular killing process of ingested organisms and/or a defect in elimination, resulting in the accumulation of partially degraded bacteria within the cytoplasm and phagolysosomes of histiocytes, forming Michaelis–Gutmann bodies around the undigested bacteria.[2] The most common infectious etiologies described are bacteria, such as *Escherichia coli*, *Rhodococcus equi*, *Pasteurella multocida*, and *Mycobacterium tuberculosis*.[2–11] Malakoplakia often occurs in immunocompromised patients, such as those with AIDS, organ transplant recipients (mostly solid organ transplants), and in one case a patient who had undergone stem cell transplantation.[5,11–14] Malakoplakia affecting a major organ could result in various organ dysfunctions. Therapy often requires surgery, which could lead to significant morbidity. One of the most serious adverse events reported was irreversible renal allograft dysfunction due to malakoplakia in a renal transplant recipient with *E. coli* infection, pyelonephritis, and bacteremia.[14] In an allogeneic stem cell transplant recipient, pleural malakoplakia caused by *R. equi*, presenting with a large tumor mass, required a lobectomy.[12] In patients with residual disease, successful results have been reported by treating the underlying infection, reducing immunosuppression, improving the bactericidal activity of monocytes with a cholinergic agonist, such as bethanechol, and administering a multivitamin supplement.[4,15,16] This is the first report of malakoplakia occurring after *M. simiae* infection.

Author Contributions

Conceived and designed the experiments: MC. Analyzed the data: MC. Wrote the first draft of the manuscript: MC. Contributed to the writing of the manuscript: MC. Agree with manuscript results and conclusions: MC, DW. Jointly developed the structure and arguments for the paper: MC, DW. Made critical revisions and approved final version: MC. Both authors reviewed and approved of the final manuscript.

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