Early Syphilis in an HIV-Infected Man Presenting With Bone Lesions and Orbital Swelling

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The clinical manifestations of syphilis are highly variable and often difficult to recognize. Secondary syphilis can produce focal involvement of various organ systems, including eye and bone. The case reported here involves secondary syphilis presenting with lytic bone lesions and unilateral lacrimal gland inflammation (dacryoadenitis) in an HIV-infected man. The lesions resolved after appropriate antibiotic therapy. While cases of syphilis osteitis have been reported in the literature, to our knowledge, this is the first case report of syphilis dacryoadenitis. [*Infect Med*. 2009;26:178-183]

Key words: Syphilis ■ HIV/AIDS ■ Dacryoadenitis ■ Osteitis

Since 1999, the number of cases of primary and secondary syphilis has increased in the United States, particularly among men who have sex with men (MSM). MSM account for two-thirds of all persons with primary and secondary syphilis in the United States.[1] In California, 60% of the MSM with primary and secondary syphilis are HIV-infected.[2] Among gay and bisexual men attending the San Francisco municipal sexually transmitted disease (STD) clinic, HIV infection, having recent "internet partners," and methamphetamine use were associated with syphilis.[3]

Identification of syphilis disease stage determines treatment and partner notification practices. The focal involvement of various organ systems includes uveitis, hepatitis, periosteitis, and meningitis, which are well-described manifestations of secondary syphilis. Bone involvement in early syphilis usually involves periosteitis of the bilateral tibias[4]; lytic bone lesions are rare. Uveitis is the most common ocular manifestation of syphilis.[5]

With the goals of increasing awareness of the wide range of systemic manifestations of secondary syphilis and reviewing public health strategies for syphilis management, we report a case of lytic cranial lesions and lacrimal gland inflammation (dacryoadenitis) caused by infection with *Treponema pallidum*. To our knowledge, this is the first reported case of syphilis-associated dacryoadenitis.

Case report

A 31-year-old man presented to the emergency department with swelling of the forehead and scalp and a right temporal headache. He sought care 1 month earlier when his symptoms began, and a CT scan of the head at that time showed no abnormalities. The patient denied fever, chills, tongue swelling, shortness of breath, and known drug allergies. He had received a diagnosis of HIV infection 2 years earlier and was antiretroviral-naive. His history also included left-sided labial paralysis secondary to Bell palsy and episodic urticaria.

The patient was born in Mexico and had been living in California since age 14 years. He worked in a restaurant and had no pets. No sexual history was obtained at this visit. His vital signs were as follows: temperature, 37.4°C (99.3°F); blood pressure, 112/63 mm Hg; pulse rate, 94 beats per minute; and respiration rate, 20 breaths per minute. Examination revealed swelling of the forehead and right temporal area, with no tenderness, erythema, or induration. Findings from the remainder of

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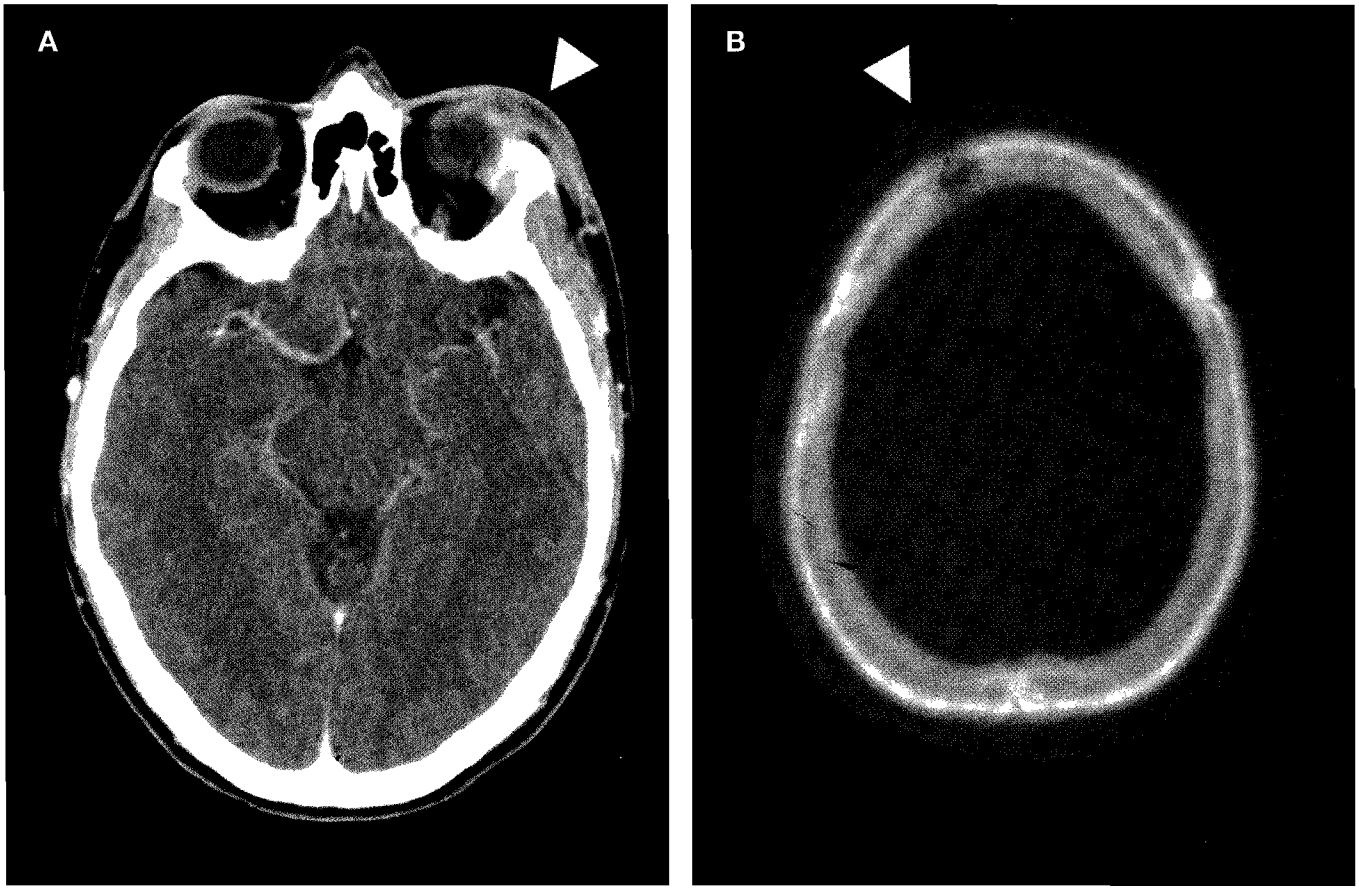

Figure – *These CT scans demonstrate unilateral lacrimal gland inflammation, or dacryoadenitis (A, arrowhead), and destructive cranial osteitis (B, arrowhead) in a patient with early syphilis and HIV coinfection.*

the examination were normal. He was treated with diphenhydramine and prednisone for a presumed allergic reaction and was discharged.

Four weeks later, the patient presented to the HIV clinic with worsening of scalp and eye swelling and headache. He reported having anal and oral sex with 3 male partners (2 of them new partners) in the past year. He was admitted to the hospital for further workup and treatment. Physical examination showed an uncomfortable man with the following vital signs: temperature, 37.4°C (99.3°F); blood pressure, 122/60 mm Hg; pulse rate, 95 beats per minute; and respiration rate, 18 breaths per minute.

Examination revealed 3 fluctuant, tender, raised masses on the right anterior scalp (3 × 3 cm), left anterior scalp (2 × 2 cm), and the back of the head (2 × 2 cm). There also was bilateral periorbital swelling, mild conjunctival injection, and mild periorbital skin erythema. The patient displayed intact extraocular movements and isocoric, light-responsive pupils. No scleral icterus or thrush was noted. His neck was supple and was without significant lymphadenopathy. The findings from his oral, skin, cardiovascular, pulmonary, abdominal, genital, and neurological examinations were all normal. In particular, he had no rashes, mucous patches, condylomata lata, or other common manifestations of secondary syphilis.

The patient's laboratory values were significant for a white blood cell count of 6900/μL, with a normal differential, and a hemoglobin level of 11.6 g/dL. Two months before admission, his $CD4^+$ T-cell count and HIV RNA level were 520/μL and 30,000 copies/mL, respectively. On admission, his $CD4^+$ T-cell count was 358/μL. Electrolyte, blood urea nitrogen, and creatinine levels and liver function test results were all normal.

A qualitative rapid plasma reagin (RPR) test that had been done 3 months earlier was nonreactive. A qualitative RPR performed during his hospitalization was found to be reactive, and a quantitative RPR test yielded a titer of 1:32. The results of a

Table – Case reports of syphilis osteitis in HIV-coinfected persons[a]

Site of osteitis	Imaging findings	Concurrent clinical findings of syphilis	Pathological findings	Age, y/gender	$CD4^+$ cell count (/μL)
Skull	CT: 3 soft tissue lesions with frontal lesion eroding through bone to epidural space	Dacryoadenitis	Dense neutrophil infiltration without granuloma formation	31/M	358
Skull	CT: multiple skull lytic lesions; MRI: 2 large masses from subcutaneous tissue to dura	Supratesticular mass resolved after syphilis treatment	Perivascular infiltration with plasma cells and lymphocytes with some necrosis	20/M	Not provided
Skull	CT: 3 lytic lesions with "worm-eaten" appearance; MRI: irregular zones of increased signal intensity on T2-weighted images and enhancement in the calvaria in areas of lytic lesions seen on CT	None	Cortical and trabecular bone with attenuated inflammatory infiltrate composed largely of lymphocytes and plasma cells	40/M	Not provided
Sternum	Chest radiograph: normal findings; CT and MRI: destructive lesion in sternal bone with small amount of surrounding fluid with peripheral enhancement	Maculopapular rash	Bone necrosis with perivascular infiltration of plasma cells and lymphocytes and rare histiocytes	20/M	251
Ulna	Ulnar radiograph: pathological fracture; bone scan: uptake in ulna as well as in asymptomatic areas of skull and radius	Maculopapular rash involving the palms and soles	Acute and chronic osteomyelitis, numerous treponemes seen on silver stain	25/M	500
Tibia	Tibial radiographs: cortical thickening of mid-diaphyseal region	Oral erythematous plaques; subcutaneous nodules on face, shins, and humerus	Perivascular granuloma consisting of epithelioid histiocytes and multinucleated giant cells surrounded by lymphocytes and plasma cells	34/F	130

M, male; F, female.

[a] Reports of syphilitic osteitis detectable only by scintigraphy (not radiologically detectable) are not included.

Reference
Present case
Gurland[8]
Huang[9]
Kandelaki[10]
Kastner[11]
Rademacher[12]

confirmatory fluorescent treponemal antibody absorption (FTA-ABS) test were positive. Angiotensin-converting enzyme level (to evaluate for sarcoidosis) was normal. The results of serological tests for *Cryptococcus* antigen, *Coccidioides* antibodies, and *Blastomyces* antibodies and tests for urinary *Histoplasma* antigen were negative.

On admission, findings on a chest radiograph were normal. CT of the head performed with and without intravenous contrast revealed left lacrimal gland swelling (dacryoadenitis) and multiple soft tissue lesions eroding through bone to the superior epidural space (Figure).

A limited craniectomy for diagnostic biopsy was performed at the site of the right frontal region where subcutaneous tissue was described as infiltrating bone. Pathological examination of the tissue demonstrated dense neutrophil infiltration without granuloma formation. Gram, Grocott-Gomori methenamine-silver, and Ziehl-Neelsen stains did not reveal any organisms. Staining with direct immunofluorescent antibody or immunoperoxidase antibody was not done because of limited biopsy tissue. Tissue sent for flow cytometry did not show evidence of malignancy. The bacterial, mycobacterial, and fungal cultures from biopsy tissue yielded no organisms.

The patient received empiric intravenous ceftriaxone and vancomycin for 1 day before the biopsy was performed. The patient was given a diagnosis of syphilitic osteitis and dacryoadenitis and was treated with aqueous penicillin, 4 million units every 4 hours for 21 days. The periorbital swelling and cranial lesions resolved after 7 days of therapy. At a follow-up visit 4 weeks after completion of therapy, a quantitative serum RPR test showed a titer of 1:4.

The local public health department provided partner counseling and referral services (PCRS) for this patient. The patient identified 3 male partners in the past 6 months, including 2 anonymous partners. One of these partners, also HIV-infected, was contacted by the local health department, tested, and found to have neurosyphilis.

Discussion

This case highlights the wide range of systemic manifestations that can occur in secondary syphilis and the importance of syphilis and HIV PCRS in public health efforts to eradicate syphilis. Despite awareness of our patient's risk factors for syphilis, the disease progressed with significant morbidity. Clinicians need to be aware of the protean manifestations of syphilis and consider the diagnosis in patients with epidemiological risk factors, such as MSM.

With this case report, we add syphilis dacryoadenitis to the ocular manifestations observed in early syphilis. Dacryoadenitis as a rare presentation of syphilis has been known for more than 100 years.[6] To our knowledge, this is the first case report to describe this condition. The lacrimal gland (located in the supratemporal orbit) may become inflamed as a result of infectious or systemic causes. Infectious dacryoadenitis is thought to be caused by ascension of an inciting agent from the conjunctiva through the lacrimal ductules into the lacrimal gland.[7]

An infectious disease differential diagnosis includes infections with viral (Paramyxovirus, Epstein-Barr virus, Cytomegalovirus, varicella-zoster virus, enteroviruses), bacterial (*Mycobacterium tuberculosis, Staphylococcus, Neisseria gonorrhoeae, T pallidum*), fungal (*Coccidioides immitis, Blastomyces dermatitidis*), and parasitic (*Taenia solium, Schistosoma)* pathogens. Noninfectious causes include sarcoidosis, Graves disease,

Sjögren syndrome, and lacrimal gland tumor.

In an HIV-infected patient such as ours, the differential diagnosis of destructive osteitis includes syphilis, tuberculosis, pyogenic osteomyelitis, deep mycoses, and lymphoma as well as non–HIV-associated inflammatory and neoplastic disorders, such as sarcoidosis, Wegener granulomatosis, and multiple myeloma. Acquired syphilitic osteitis in HIV-coinfected persons has been reported infrequently (Table).[8-12] In these patients, osteitis occurred with an anatomical distribution similar to that of cases reported in non–HIV-infected persons,[13] with most lesions involving the skull and, less frequently, the sternum and long bones.

On the basis of case reports of early syphilis in HIV-coinfected patients,[14] it is tempting to conclude that an impaired cellular immune system exacerbates the severity of the clinical presentation of syphilis. While some authors have described a more malignant course of syphilis in HIV-infected patients,[14] a CDC-sponsored prospective, randomized, controlled trial involving HIV-infected and uninfected outpatients found that HIV infection had a minimal effect on the clinical manifestations of early syphilis.[15]

Reports of standard treatment failure in HIV-coinfected patients and the possibility of spirochete sequestration in areas such as bone, where adequate levels of penicillin are difficult to achieve, led us to treat our patient with an extended course of intravenous penicillin. For treatment of syphilitic eye infections (specifically, uveitis, neuroretinitis, and optic neuritis), the CDC recommends 18 to 24 million units of aqueous crystalline penicillin G for 10 to 14 days. Many experts recommend that at the conclusion of this therapy, patients receive 2 or 3 weekly doses of benzathine penicillin G to eliminate the risk that latent forms of syphilis will persist.[16]

For HIV-coinfected persons, follow-up of nontreponemal titers at 3, 6, 9, 12, and 24 months after treatment for syphilis is important for monitoring treatment effectiveness and the possibility of relapse or reinfection. A 4-fold decrease in titer (from 1:64 to 1:16) by 6 to 12 months of follow-up is considered an appropriate response to therapy.[16] Retreatment should be considered if clinical signs and symptoms of syphilis persist or recur or if the nontreponemal titer persists or increases.[17] One study found that serological responses to treatment were worse among 541 HIV-infected patients with primary and secondary syphilis than in non–HIV-infected patients, although this impaired response to therapy was not found to be clinically significant.[18]

All probable or confirmed cases of early syphilis and all reactive nontreponemal laboratory test results should be reported to the local health department within 1 working day by public and private providers and laboratories.[19] Syphilis is an ideal candidate for partner notification, screening, and prophylaxis efforts given its well-characterized prolonged incubation period during which infection can be prevented with penicillin G therapy. The elicitation of and testing periods for at-risk sexual partners, preferably by the local health department, varies depending on the stage of syphilis.

All sexual partners within 3 months of a diagnosis of primary, secondary, or early latent syphilis in an index case should, at a minimum, be treated presumptively with a single intramuscular dose of benzathine penicillin G. For secondary syphilis, all sexual partners within the past 6 months should be identified.[16] HIV-infected persons should have access to PCRS not only at initial diagnosis of HIV infection but also if new partners are exposed in the future, as suggested by incident STD diagnosis.[20]

Sexually active MSM with risk factors (multiple or anonymous partners, sex in conjunction with illicit drug use, or sexual partners who have these risk factors) should be tested for syphilis at 3- to 6-month intervals. Sexually active MSM who do not have these risk factors should be tested at least annually.[16]

All HIV-infected men or women should have syphilis serological testing at the initial visit. Annual or more frequent (every 3 to 6 months) syphilis serological screening is indicated for all HIV-infected persons, with frequency determined by periodic risk assessment.[21]

In addition to routine screening of populations at-risk for syphilis and knowledge of the protean manifestations of syphilis, clinicians need to promote PCRS efforts in their local health jurisdictions to improve access to testing and treatment for at-risk partners. ❖

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