Cutaneous Tuberculosis of the Penis and Sexual Transmission of Tuberculosis Confirmed by Molecular Typing

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A case of culture-positive primary cutaneous Mycobacterium tuberculosis infection of the penis was diagnosed in a male patient; 1 year later, endometrial tuberculosis was diagnosed in the patient’s wife. These organisms were confirmed to be indistinguishable by use of molecular techniques.

Extrapulmonary tuberculosis is a relatively uncommon condition in the developed world. It is occasionally associated with other serious underlying disease, such as HIV infection, and reflects different modes of transmission. The mechanisms leading to extrapulmonary tuberculosis include lymphatic and hematogenous transmission, local transmission, ingestion of organisms, and direct inoculation. We describe a patient with culture-positive primary cutaneous tuberculosis and the subsequent diagnosis of endometrial tuberculosis in the patient’s wife.

Case 1. A 50-year-old Indian man was referred by his general practitioner; the patient had had a painless nodule or ulcer on his penis for 2 months. The lesion appeared shortly after he had returned from a visit to India. He initially noticed a small lump on his penis that had gradually increased in size. The lump was painless, and the patient had no other local or systemic symptoms. He was married and denied having had any other sex partners for >25 years. He used no contraception. He drank approximately 50 U of alcohol per week and was a smoker. He had lived in the United Kingdom for >40 years.

On examination (figure 1), an indurated ulcer of 1 cm in diameter 1 cm in depth was present immediately adjacent to the penile corona. It was firm and nontender, and it had a rolled edge (figure 1). Small, mobile, nontender, left inguinal nodes could be palpated. He had no other lymphadenopathy or skin lesions. Examination of the other systems yielded normal findings. A BCG scar was present on his arm. An urgent punch biopsy was performed to exclude malignancy. The histopathology report was of granulomas with no cause identified. Gram, Ziehl-Neelsen, Giemsa, and fungal stains all yielded negative results. The serum rapid plasma reagin test and Treponema pallidum hemagglutination assay twice yielded negative results. The patient did not consent to an HIV test. Three urine samples obtained during the early morning were microscopically negative and culture-negative for mycobacteria, and results of cytological testing were negative. The findings on a chest radiograph and abdominal ultrasound were normal. In the absence of a diagnosis, an excision biopsy was performed to get additional tissue specimens for culture. The histopathology report on the excision biopsy specimen showed caseating granulomas with no cause identified, and again microbiology stains all yielded negative results. Culture on Löwenstein-Jensen medium yielded Mycobacterium tuberculosis that was susceptible to isoniazid, rifampicin, pyrazinamide, streptomycin, and ethambutol.

Treatment was commenced with isoniazid (300 mg/day), rifampicin (600 mg/day), pyrazinamide (2 g/day), and pyridoxine (10 mg/day) for 2 months, followed by isoniazid and rifampicin for a further 4 months. The excision biopsy site healed with no recurrence of the skin lesion. The family was screened by the Public Health Department (Oxfordshire Health Authority, United Kingdom), and no other cases of tuberculosis were identified. His wife refused to attend the genitourinary medicine department for examination and screening.

Case 2. A 49-year-old Indian woman, para 2 + 0, presented to the gynecologist with a 3-month history of menorrhagia, fever, sweats, and weight loss. An endometrial novethisterone biopsy was performed, and the patient was given norethindrone tablets to control the bleeding. The biopsy specimen revealed multiple caseating granulomas with no cause identified, and she was referred to the infectious diseases department. She had been in the United Kingdom for 14 years and had a history of pelvic inflammatory disease, with removal of an intrauterine contraceptive device in 1992 and again in 1997. She did not remember having had tuberculosis in the past, but she said that her husband had been treated for penile tuberculosis 1 year previously. On examination, she looked healthy and had a whitish, odorless vaginal discharge with some cervical ulceration. Swabs were taken and arrangements were made for an additional novethisterone biopsy to obtain material for culture. Laboratory findings were
unremarkable, with an erythrocyte sedimentation rate of 3 mm/h and C-reactive protein level of <8 mg/L (normal, 8 mg/L). HIV and hepatitis B tests, rapid plasma reagin testing, and *T. pallidum* hemagglutination assay yielded negative results. Results of the urine dipstick test were negative. Chest radiography revealed a calcified granuloma in the left apex with no active lesions seen; the findings of abdominal ultrasound were normal. Cultures of urine samples obtained during the early morning and of vaginal swabs yielded negative results; however, culture of the second biopsy specimen yielded *M. tuberculosis* that was susceptible to isoniazid, rifampicin, pyrazinamide, streptomycin, and ethambutol.

Both of the cultured samples were sent to the Public Health Laboratory *Mycobacterium Reference Laboratory in Dulwich, United Kingdom. They confirmed the identification and sensitivities of the organism. Restriction fragment length polymorphism analysis based on the IS6110 insertion element showed the organisms from the 2 cases to be identical, with all 14 bands similar. This technique has been shown to be more discriminatory than spoligotyping in outbreak investigations [1].

**Discussion.** Cutaneous tuberculosis is well described in patients with and without underlying tuberculosis in other parts of the body, when either local infection (such as in prospector’s wart), local spread, or hematogenous dissemination from a pulmonary focus is thought to give rise to the cutaneous lesion. The most common lesion is probably lupus vulgaris. Culture for *M. tuberculosis* from these specimens of lesions almost always yields negative results [2], and molecular techniques may be more appropriate [1, 3].

Penile tuberculosis is extremely rare, whereas tuberculosis of the epididymis or testes is more common. In 1848, Fournier described the first case of a patient with multiple penile ulcers and regional lymphadenopathy [4]. Lewis [4] reviewed 110 cases in the literature before 1946. Lal et al. [5] reviewed 29 cases occurring from 1946 through 1971. From 1971 through 1992, an additional 16 cases have been described in the literature [6–19]. Konohana et al. [20] provided the first report of a culture-positive penile tuberculosis lesion in 1992, which involved a 63-year-old Japanese man who had recently undergone treatment with intravesical BCG, but whose penile lesion was nonetheless shown to be culture-positive for *M. tuberculosis*. Recently, other mycobacteria, such as *Mycobacterium avium-intracellulare* [21] and *Mycobacterium celatum* [22], have been reported to cause penile lesions. Patients with penile tuberculosis can present with impotence [13, 16], and sexual transmission has also been recently reported [15].

We believe that our patient represents only the fourth report of culture-positive penile tuberculosis [15, 18, 20]. This is also the first report to confirm, by means of molecular biological techniques, that sexual transmission has occurred. Although the husband declined an HIV antibody test, he had no clinical features to suggest underlying immunosuppression, and his wife was negative for HIV and hepatitis B surface antigen. There was no evidence of pulmonary or renal tract tuberculosis on ultrasound. He denied having had any other sexual contacts apart from his wife, and results of routine screening for active tuberculosis by chest radiography of the family were negative. He had a scar on his upper arm compatible with a previous BCG vaccination.

The historical literature describes penile tuberculosis as arising rarely from sexual contact with an infected partner or contamination from infected clothing [4]. In the 19th century, it was described most frequently in Jewish infants who had undergone ritual circumcision [23]. After performing the circumcision, the religious leader would suck the bleeding penis. Extrapulmonary tuberculosis is not generally regarded as being infectious, but because transmission from one mucosal surface to another during intercourse is at least a theoretical possibility, and because it has been described in animal models [24, 25], we advised the patient not to have intercourse until at least 1 month of therapy had been completed, as suggested elsewhere.
[26]. We treated this patient with antituberculosis chemotherapy for 6 months.

The differential diagnosis of a chronic penile ulcer with histological features of granulomas is extensive. Consideration needs to be given to bacterial and fungal infections, parasitic infections, vasculitides, inflammatory bowel disease, sarcoid, and foreign body reactions. Because there is a paucity of organisms present in most forms of cutaneous tuberculosis, with the exception of scrofuloderma and cutaneous miliary tuberculosis, results of both staining and culture are usually negative.

In an attempt to overcome this problem, a number of workers have successfully used PCR to detect *M. tuberculosis* DNA in cutaneous lesions. We have used these techniques to show sexual transmission.

Primary cutaneous penile tuberculosis is an extremely rare condition, and we believe that this is only the fourth culture-positive case report in the world literature. We have shown sexual transmission between patients with asymptomatic endometrial tuberculosis and a tuberculous penile ulcer by means of molecular methods. It is not possible to say exactly how transmission occurred. This emphasizes the importance of screening sex partners in high-risk groups for diseases that are not traditionally transmitted sexually.

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**References**


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