Donovanosis (also known as granuloma inguinale) is a major cause of genital ulcers in many tropical regions of the world, including southeast India, Brazil, the Caribbean, Papua New Guinea, northern Australia, and eastern South Africa [1, 2]. Historically, most cases of donovanosis in the United States have originated in the Southeast or have occurred in immigrants in New York City. However, from 1990 to 1994, more than one-half of the 160 cases notified in the United States were from Texas or California [3–7].

Donovanosis is due to Calymmatobacterium granulomatis, a gram-negative bacillus probably related most closely to Klebsiella species. Donovanosis is underrecognized because of its susceptibility to antibiotics in many classes (except the penicillins), confusion with other causes of genital ulcer disease, and difficulties with diagnostic testing for the organism. In 1996, the first isolation of C. granulomatis in >30 years was described [8].

Donovanosis usually begins as a small firm painless papule on the external genitalia that may ulcerate to form a characteristic beefy-red fleshy exuberant ulcer, which bleeds profusely on touch [1]. Chronic subcutaneous spread of the infection may occur. Lymphadenopathy is usually absent, although tender inguinal lymph nodes may be palpated if the ulcers become secondarily infected. If untreated, the ulcerative lesions may become quite destructive or deforming. Lymphatic obstruction leading to elephantiasis of the external genitalia has been well described [9]. However, asymptomatic lesions of the vaginal wall and cervix can also occur, which may be detectable only by observation of characteristic Donovan bodies in Papanicolaou smears.

Since cultivation of the organism is so difficult, demonstration of the typical Donovan bodies on stained smears is widely regarded as the gold standard of diagnosis [1]. Although Giemsa stain is probably the most widely used stain to demonstrate Donovan bodies, Warthin-Starry, Papanicolaou’s, and silver stains can also be used. Donovan bodies are C. granulomatis organisms seen within the cytoplasm of mononuclear cells. Sometimes the organisms appear as diplococcoid forms, resembling a closed safety pin [1].

Although donovanosis is primarily a disease of the genitals, extragenital sites of infection can occur [10]. In this article, extragenital infection affecting the thoracic vertebrae with subsequent spinal cord compression is described, and the previously reported cases of donovanosis involving bone are reviewed.

Methods

Cases of bony disease due to donovanosis (granuloma inguinale) that were reported from 1966 to 1997 were identified through a MEDLINE search. The key phrase utilized in the search was “granuloma inguinale.” Reference lists of the identified articles were reviewed to find additional cases.

Case Report

A 54-year-old woman from the Torres Strait Islands between northern Australia and Papua New Guinea was referred to a tertiary referral center for radiotherapy for a presumed malignant lesion involving the midthoracic vertebrae. She had a history of alcoholism and diabetes mellitus and had been admitted to a hospital in the Torres Strait Islands 1 month before because of pneumonia. During this illness, she had fever, night sweats, cough, and malaise. No etiologic agent of pneumonia...
was found, but upon recovery, she was found to have difficulty walking. Radiological investigations revealed a destructive lesion of the fourth and fifth thoracic vertebrae that caused spinal cord compression.

Upon transfer to the tertiary referral center, radiotherapy was deferred pending results of histological examination. MRI (figure 1) confirmed the previous radiological diagnosis. Examination of her back revealed gross kyphosis but no evidence of skin ulcer. The patient was afebrile. She was unable to walk and had neurological signs consistent with a midthoracic spinal cord lesion. Skin testing showed that she was anergic.

Open biopsy of the body of the fourth thoracic vertebra was performed. Histological examination of the excised bone revealed fibropurulent exudate, necrotic debris, new bone and osteoid, and fibrous scar tissue. Collections of macrophages were seen within the fibrous tissue. Hematoxylin-eosin staining showed small blue round bodies within the cytoplasm of the macrophages, a finding consistent with Donovan bodies. Gram staining showed that these bodies were gram-negative. Warthin-Starry staining and Grocott-Gomori methenamine–silver nitrate staining were positive.

Histological examination revealed a diagnosis of donovanosis. Bacterial, fungal, and mycobacterial cultures did not yield organisms. No attempts were made to culture C. granulomatis. Further evidence to support the diagnosis of donovanosis included her residence in an area in which the disease is endemic.

The patient had no recollection of genital ulceration. Physical examination revealed no genital lesions. There was evidence that she had undergone a total hysterectomy. According to the patient, this procedure had been performed ~10 years before because of menorrhagia. Operation notes were not available, and neither the patient nor the referring physician was able to specify whether a cause had been found for menorrhagia.

Treatment was commenced with doxycycline (100 mg every 12 hours by mouth). After 6 weeks of this therapy, minor neurological improvement had occurred. The patient refused follow-up MRI. She returned to her local community in the Torres Strait Islands, where she died of hypostatic pneumonia as a complication of her paraparesis. An autopsy was not performed.

Discussion

The 54-year-old woman described in this report had an unusual manifestation of an infectious disease that is unusual in developed countries. Multiple cases of autopsy-proven extragenital donovanosis were described in the first half of this century before the availability of effective therapy against C. granulomatis [10, 11]. However, since the advent of chloramphenicol, streptomycin, sulfur-based antibiotics, and tetracyclines, extragenital donovanosis has become a rarity. Extragential lesions usually affect the mouth, skin, or bone, although other sites may sometimes be affected. Previously reported cases of disseminated bony disease are summarized in table 1. Bony involvement due to direct extension from local sites of the disease such as the anus and rectum [27], mouth [28], and skin [15, 29, 30] has also been described.

Six previous cases of vertebral disease have been described; five were disseminated disease [12, 17, 18, 24] and one was due to direct extension from an anorectal mass [27]. The patient described in this report was thought to have a malignancy on the basis of both clinical and radiological grounds. Her bony disease was consistent radiologically with destructive osteolytic metastatic deposits or multiple myeloma. However, there was no evidence of a primary malignancy, and the serum electrophoretic pattern excluded multiple myeloma. An infectious etiology was also thought possible; therefore, surgical specimens were cultured for aerobic and anaerobic bacteria, mycobacteria,

![Figure 1](https://academic.oup.com/cid/article-abstract/26/2/379/508229)
### Table 1. Summary of data on cases of disseminated donovanosis involving bone.

<table>
<thead>
<tr>
<th>Case no., age (y)/sex</th>
<th>Country</th>
<th>Site(s) of infection</th>
<th>Concomitant genital lesion (location)</th>
<th>Treatment (outcome)</th>
<th>[Reference(s)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 54/F</td>
<td>Australia</td>
<td>Thoracic spine</td>
<td>No</td>
<td>Doxycyline (died)</td>
<td>[PR]</td>
</tr>
<tr>
<td>2, NS/NS</td>
<td>NS</td>
<td>Lumbar spine</td>
<td>NS</td>
<td>None (died)</td>
<td>[12]</td>
</tr>
<tr>
<td>3, 45/F</td>
<td>Australia</td>
<td>Ilium</td>
<td>No</td>
<td>Tetracycline (cured)</td>
<td>[13]</td>
</tr>
<tr>
<td>4, 41/F</td>
<td>Australia</td>
<td>Ulna, tibiae, metatarsals</td>
<td>Yes (introitus)</td>
<td>Tetracycline (cured)</td>
<td>[14]</td>
</tr>
<tr>
<td>5, 15/M</td>
<td>New Guinea</td>
<td>Tibia</td>
<td>Yes (penis)</td>
<td>Chloramphenicol (unknown)</td>
<td>[15]</td>
</tr>
<tr>
<td>6, 27/F</td>
<td>Guatemala</td>
<td>Knee joint</td>
<td>Yes (vulva)</td>
<td>Tetracycline (cured)</td>
<td>[16]</td>
</tr>
<tr>
<td>7, 20/F</td>
<td>Jamaica</td>
<td>Radius, lumbosacral spine, tibia, fibula</td>
<td>Yes (vulva)</td>
<td>Tetracycline (cured)</td>
<td>[17]</td>
</tr>
<tr>
<td>8, 48/F</td>
<td>United States</td>
<td>Lumbar vertebra</td>
<td>Yes (cervix)</td>
<td>Chloramphenicol (cured)</td>
<td>[18]</td>
</tr>
<tr>
<td>9, 50/F</td>
<td>Venezuela</td>
<td>Lumbar vertebra, sacrum</td>
<td>Yes (cervix)</td>
<td>Streptomycin, chloramphenicol (died)</td>
<td>[17]</td>
</tr>
<tr>
<td>10, 21/F</td>
<td>India</td>
<td>Tibia, radius</td>
<td>Yes (cervix)</td>
<td>Tetracycline (cured)</td>
<td>[19]</td>
</tr>
<tr>
<td>11, 22/F</td>
<td>United States</td>
<td>Clavicle, tibia</td>
<td>Yes (cervix)</td>
<td>Streptomycin (cured)</td>
<td>[20]</td>
</tr>
<tr>
<td>12, 20/F</td>
<td>United States</td>
<td>Tibia, both radii</td>
<td>Yes (cervix)</td>
<td>Streptomycin (cured)</td>
<td>[17]</td>
</tr>
<tr>
<td>13, 19/F</td>
<td>United States</td>
<td>Tibia, feet</td>
<td>Yes (cervix)</td>
<td>Antimony (cured)</td>
<td>[21]</td>
</tr>
<tr>
<td>14, 33/F</td>
<td>United States</td>
<td>Tibia, fibula, ulna, radius, talus, skull</td>
<td>Yes (cervix)</td>
<td>None (died)</td>
<td>[22]</td>
</tr>
<tr>
<td>15, 48/M</td>
<td>United States</td>
<td>Tibia, ribs</td>
<td>Yes (penis)</td>
<td>Sulfadiazine (cured)</td>
<td>[23]</td>
</tr>
<tr>
<td>16, 20/F</td>
<td>United States</td>
<td>Multiple (small bones of hands and feet; tibia; fibula; ulna; skull; clavicle)</td>
<td>Yes (cervix)</td>
<td>Sulfadiazine (died)</td>
<td>[24]</td>
</tr>
<tr>
<td>17, 19/F</td>
<td>United States</td>
<td>Lumbar vertebrae, femoral head</td>
<td>No</td>
<td>Tartar emetic (died)</td>
<td>[24]</td>
</tr>
<tr>
<td>18, 16/F</td>
<td>United States</td>
<td>Clavicle, radius, ulna, metacarpals</td>
<td>No</td>
<td>Amputation of upper limbs (cured)</td>
<td>[24]</td>
</tr>
<tr>
<td>19, 21/F</td>
<td>United States</td>
<td>Scapula, ribs</td>
<td>Yes (cervix)</td>
<td>Antimony (died)</td>
<td>[25, 26]</td>
</tr>
</tbody>
</table>

**NOTE.** NS = not stated; PR = present report.

Culture of *C. granulomatis* is extremely difficult, although a monocyte coculture system has been recently used successfully [8]. Skin tests and serological tests for donovanosis have been available in the past but are of dubious specificity. Molecular-based detection methods are in development in some centers but have not yet been standardized or commercially released. These molecular tests may prove to be an important adjunct to staining in the future.

Radiologically, the bony lesions of donovanosis can be confused with many other conditions. In addition to previously mentioned possibilities (tuberculosis, metastatic malignancy, and coccidioidomycosis), metaphyseal fibrous defects, multiple myeloma, leukemia, or syphilitic gumma may also be part of the radiological differential diagnosis. Bony lesions are osteolytic [17]. Although sclerosis around the periphery of the lesion may occur in long-standing cases, there is little marginal reaction in the early stages of the disease. Periosteal reaction may develop during the healing phase. When long bones are affected (involvement of the tibia has been described in 50% of previously reported cases), the lesions tend to be metaphyseal [17]. Usually, but not always [22], cancellous rather than cortical bone is affected.

Patients with disseminated bony disease usually, but not always, have systemic symptoms such as weight loss, fever,
night sweats, and malaise [10]. The patient described in this case report had constitutional symptoms associated with her initial presentation, but these symptoms had resolved by the time she was referred to the tertiary referral hospital. It is possible that antibiotic treatment of her pneumonia may have also resolved systemic symptoms associated with her disseminated donovanosis.

The patient in this report had no recollection of genital ulcer disease that was consistent with donovanosis. It is possible that she had vulval lesions that resolved with antibiotic treatment of her pneumonia. It appears more likely that she had previous cervical donovanosis. Although she had undergone a hysterectomy reportedly for treatment of menorrhagia, the surgery notes are no longer available, and it is possible that unsuspected cervical donovanosis was present at the time of the operation. Cervical donovanosis macroscopically resembles squamous cell carcinoma of the cervix. In addition, untreated cervical donovanosis may invade or compress adjacent pelvic structures, as does cervical cancer [10]. It could be speculated that the hysterectomy was performed for treatment of suspected locally invasive carcinoma of the cervix.

It is interesting that all but two of 17 previously reported cases of disseminated donovanosis involving bone were in females, and in 10 of the 15 cases in females demonstrable disease affected the cervix. Dissemination is more likely in patients who have cervical disease because the disease goes unnoticed and untreated probably for several years. In addition, operative procedures (including biopsy) may increase the risk of dissemination by allowing easy entry of organisms into the bloodstream [17]. This patient’s hysterectomy, while removing macroscopic evidence of the infection, may have facilitated blood-borne spread of C. granulomatis. It has also been suggested that pregnancy increases the risk of dissemination by similar mechanisms [17], but this suggestion has been recently disputed [31]. It is more likely that systemic spread is facilitated by delivery or abortion.

Optimal treatment of bony disease due to donovanosis has not been established. For many years, tetracycline has been regarded as the drug of choice for treatment of donovanosis, although trimethoprim-sulfamethoxazole, chloramphenicol, and streptomycin have also been successfully used. In some previously reported cases of extragenital donovanosis, tetracycline therapy failed, but trimethoprim-sulfamethoxazole treatment effected rapid cure [32–34]. The patient described in the present report had only limited clinical improvement with doxycycline therapy, although the absence of radiological follow-up makes assessment of response difficult. Her lack of clinical response may have been due to prolonged spinal cord compression rather than to failure of antibiotic therapy. The extent of bone penetration of this drug in adults is not known, but five previously reported cases of bony disease have been successfully treated with tetracyclines [13, 14, 16, 17, 19].

Azithromycin is emerging as probably the most useful drug with which to treat either genital or extragenital donovanosis. Preliminary clinical trials of azithromycin as treatment of extensive genital disease have shown dramatic success [35, 36]. Advantages of azithromycin include concentration within macrophages and a pharmacokinetic profile allowing compliance with treatment protocols. The optimal regimen of azithromycin therapy for bony disease is unknown, but daily therapy for a short period (e.g., 7 days) followed by once weekly therapy for at least 4–6 weeks may be a possible regimen.

Disease of bone due to donovanosis is rare but needs to be considered in the differential diagnosis of osteomyelitis (especially that presumed to be tuberculous) or bone disease presumed to be due to malignancy, especially for patients coming from areas of endemicity or those with genital tract abnormalities (whether considered due to donovanosis or other processes). The outcome is good if the diagnosis is established early; fatal cases mainly occur because of misdiagnosis. Given the association between primary lesions of the uterine cervix and disseminated bony disease due to donovanosis, thorough and early pelvic examinations should play a role in decreasing the morbidity and mortality due to donovanosis.

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References


