Extragenital Donovanosis with late diagnosis. A case report

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Background: Donovanosis is an infection caused by Klebsiella granulomatis, which produces genital ulcers. However, it also has various forms of presentation and can sometimes cause rare conditions such as extragenital or systemic presentation. Although it is very rare, it can transform malignantly into squamous cell carcinoma. This pathology was described in 1882 by McLeod, and in 1905, Charles Donovan identified the causal agent of the disease. This microorganism was initially considered a protozoan, but it was later discovered to be a bacterium.

We report a clinical case of extragenital donovanosis treated at the New General Hospital of Gómez Palacio Durango, treated successfully with antibiotic therapy.

Donovanosis is a rare disease. Mainly endemic in countries such as Papua New Guinea, South Africa, parts of India and Brazil, and among the Aboriginal community of Australia, sporadic cases have also been reported in other South American countries. Given its low frequency, it is important to be aware of this disease in order to make a timely diagnosis and treatment.

Keywords: Granuloma Inguinale, Calymmatobacterium

Case Report

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Donovanosis is a chronic, progressive, and indolent sexually transmitted infection of the skin and anogenital mucosa caused by Klebsiella granulomatis. It manifests as granulomatous ulcers that rarely heal spontaneously.[1] Several authors have described its possible malignant transformation to squamous cell carcinoma[2,3,4]; however, it is a rare complication that occurs in long-standing ulcers, with an incidence of approximately 0.25%.[5]

The disease was first described in 1882 by McLeod in Calcutta.[6] In 1905, Charles Donovan, working in Madras (present-day Chennai), identified the etiologic agent by observing intracellular inclusions in macrophages in the lesions, now known as "Donovan bodies."[7] In 1913, Aragão and Viana introduced intravenous treatment with tartar emetic (the first effective treatment) and proposed the name *Calymmatobacterium granulomatis* for the organism.[8] Subsequently, McIntosh demonstrated the transmissibility of the disease through subcutaneous implants in volunteers,[9] and in 1939 Greenblatt et al. reproduced the infection with pseudobuboe material, although without success in culturing it in poultry embryos.[10]

In 1943, Anderson isolated the organism from the yolk sac of poultry embryos and suggested the species *Donovania granulomatis*; a few years later, Marmell and Santora coined the term "donovanosis" in Donovan's honor.[11] Jardim published the first widely accepted clinical classification in 1987.[12] Finally, phylogenetic studies by Carter et al. in 1999 demonstrated the close relationship of the pathogen with the genus Klebsiella, so it was reclassified as *K. granulomatis.*[13]

We present a case of extragenital donovanosis treated at the Nuevo Hospital General de Gómez Palacio (Durango, Mexico); due to its unusual location, we emphasize the need for early diagnosis and appropriate treatment to avoid serious complications. The diagnosis was confirmed by skin biopsy and Giemsa staining with visualization of Donovan bodies.

Case report

A 31-year-old male textile industry employee with no chronic comorbidities or substance abuse presented with a 17-month history of dermatosis located on the lower left quadrant of the abdomen. The lesion began as erythematous papules that coalesced to form an irregular 9 × 6 cm plaque composed of firm nodules and superficial ulcers; the surface was friable, with serosanguinous exudate and a brown pigmented halo at the periphery.

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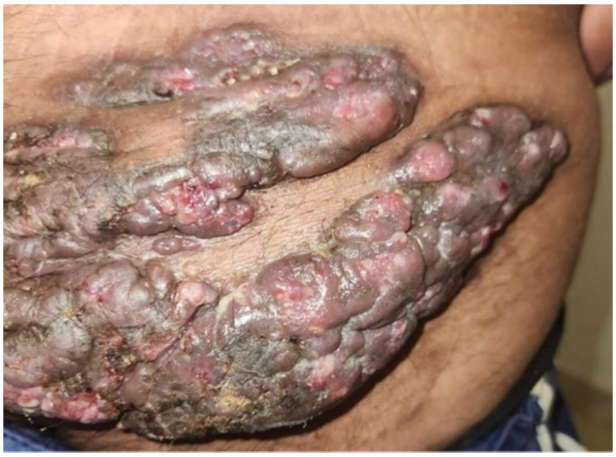

Figure 1. Abdominal extragenital Donovanosis. Ulcerative infiltrative plaque in the lower left quadrant: coalescent nodules with a reddish verrucous-granular surface, with foci of superficial hemorrhage and peripheral hyperpigmented halo.

During the first eight months, he was treated in a private practice with amoxicillin, clindamycin, and ceftriaxone without improvement. During this time, he experienced weight loss of 40 kg and progression of the plaque with persistent purulent and bloody discharge.

First hospital evaluation (month 9)

- **Incisional biopsy (General Surgery Department):** acanthotic epidermis with pseudoepitheliomatous hyperplasia, neutrophilic microabscesses, and a dense plasmacytic infiltrate in the dermis; no identifiable pathogen.
- **Laboratory tests:** blood glucose 90 mg/dL, HbA1c 5.1%, normal blood count; HIV and VDRL serology were nonreactive; chest x-ray was normal.

The patient was discharged with topical dressings and an open appointment; he did not return for immediate follow-up.

Second hospital evaluation (month 15)

She was admitted to the Internal Medicine Department with intermittent fever, occasional epistaxis, anorexia, and mild confusion. The physical examination revealed:

- **Abdominal dermatosis:** ulcerated plaque described, now 12 × 8 cm, with raised edges, granular bed and easy bleeding **(Figure 1)**.
- **Adenomegaly:** multiple painful inguinal lymph nodes **(Figure 2)** and right axillary adenopathy measuring 12 × 8 cm **(Figure 3)**.

Contrast-enhanced abdominal and pelvic CT scan: homogeneous liver; portal vein diameter 15–16 mm; splenomegaly 16 × 7.6 cm; bilateral retroperitoneal and inguinal lymphadenopathy.

Definitive diagnostic biopsy: A new biopsy of the abdominal lesion was performed.

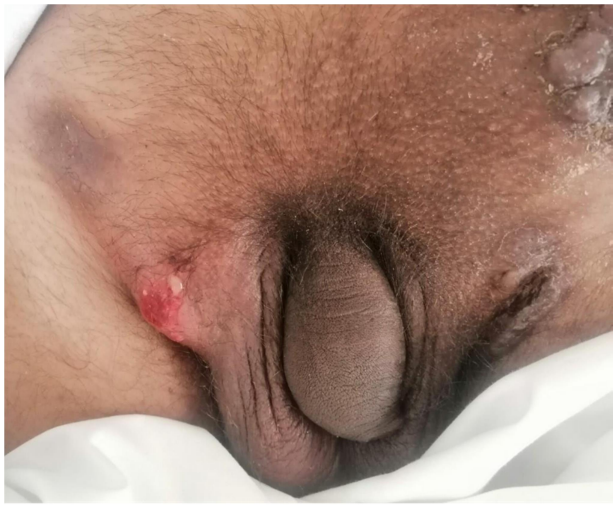

Figure 2. Inguinal lesion associated with abdominal Donovanosis. Erythematous-ulcerated papule in the right scrotal fold (pseudobubo), representative of regional lymphatic dissemination.

- **Histology showed:** Superficial and deep dermis with vacuolated histiocytes filled with intracytoplasmic microorganisms, micro-abscesses and multinucleated giant cells.
- **Giemsa stain:** macrophages with abundant Donovan bodies **(Figure 4)**.

Treatment and evolution

Doxycycline 100 mg orally every 12 hours for 6 weeks was started. By the third week, the lesion was observed to have decreased exudate and bleeding, with progressive reduction in plaque size and lymphadenopathy.

At the 8-week follow-up, the lesion was epithelialized and the patient was free of systemic symptoms. He remains under outpatient follow-up with no recurrence at 6 months.

Discussion

Donovanosis is a tropical ulcerative infection caused by *Klebsiella granulomatis*.[14] Although McLeod described it in Calcutta in 1882 [6] and Donovan identified "Donovan bodies" in 1905 [7], its clinical relevance persists due to the morbidity of the chronic ulcers it causes.

The agent was initially named *Calymmatobacterium granulomatis*; phylogenetic analysis demonstrated ≥99% similarity to *K. pneumoniae* and *K. rhinoscleromatis*, and it was reclassified as *K. granulomatis*.[15] Morphologically, it is an intracellular Gram-negative coccobacillus measuring 0.2–0.5 µm (coccobacillus) or 1.0–2.5 µm (bacillary).[16]

Endemic areas include Papua New Guinea, KwaZulu-Natal (South Africa), parts of India and Brazil, and Australian Aboriginal communities; outbreaks have also been reported in the Caribbean

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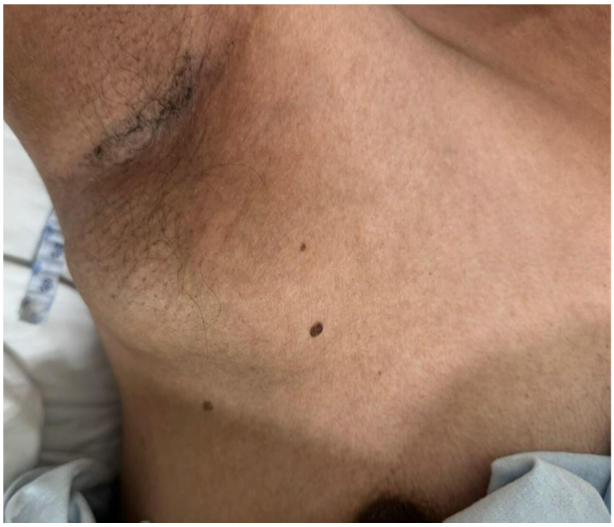

Figure 3. Right axillary adenopathy. Subcutaneous oval mass that thins the overlying skin without ulceration, corresponding to lymphatic extension of Klebsiella granulomatis.

and South America.[17] An Australian eradication program virtually eliminated the disease in that country.[18] In Papua New Guinea, 10,000 cases were documented between 1922 and 1952,[19] and in Durban, 3,153 cases in 1997 alone.[20,21] In Latin America, series from Argentina,[22] Peru,[23,24] Brazil,[25] and Paraguay have been published.[26] There are no previous Mexican reports, which justifies the presentation of this case.

It primarily affects adults aged 20–40 years; pediatric cases are rare and are usually associated with close contact with infected adults.[27] Although it is recognized as a sexually transmitted infection (STI), autoinoculation or fecal contamination of traumatized skin has also been described.[28]

Before 1947, 72% of authors denied sexual transmission; later, the figure fell to 8%.[29] Arguments in favor of sexual transmission include recent sexual history, anal lesions in men who practice receptive anal sex, and coexistence with other STIs; arguments against include childhood cases, absence in many sexual partners, and extragenital primary lesions.[30] Bleeding ulcers facilitate HIV transmission, so screening is mandatory.

Degeneration to squamous cell carcinoma is rare (<0.03%) and is associated with long-standing ulcers unresponsive to antibiotics, necessitating biopsy in persistent lesions.[31,32,33]

The incubation period ranges from 1 to 365 days.[34] Clinical studies commonly estimate it to be between 17 and 40 days,[35] with an average of 3 and 40 days in 92% of patients.[14] Ninety percent of cases affect the genitals and 10% the inguinal region; extragenital involvement accounts for 6%.[36]

The disease begins with a papular lesion or subcutaneous nodule that evolves into an ulceration with a papular surface or subcutaneous nodule at the inoculation site. The surface ulceration is

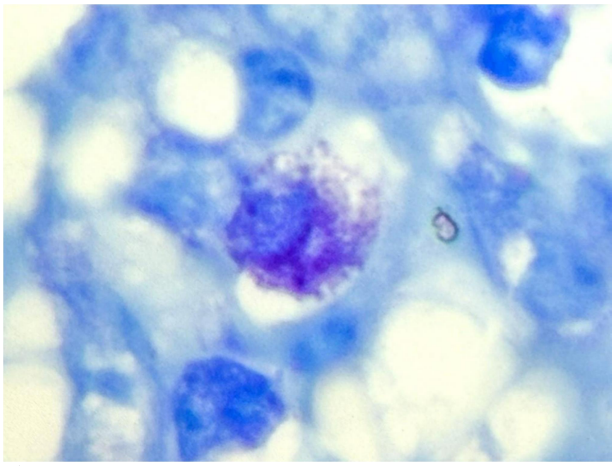

Figure 4. Donovan bodies.

erythematous, shiny, friable, and slow-growing. The lesions are generally painless, and there are no inguinal lymphadenopathy; however, the initial lesions on inguinal topography resemble a bulb (pseudobulb). As the disease progresses, the clinical manifestations are linked to the effectiveness of the host immune response, leading to local manifestations in the vast majority of patients and occasionally to visceral lesions due to hematogenous spread.[37]

The classification proposed by Jardim in 1987 is mentioned in Table 1.[12]

The 2016 European guideline adds necrotic and sclerotic/cicatricial forms.[36] Our patient presented with an extragenital form with retroperitoneal lymphadenopathy and splenomegaly.

The differential diagnosis of Donovanosis includes syphilitic chancre, soft chancre, lymphogranuloma venereum, chronic herpetic ulcer, cutaneous tuberculosis, cutaneous amebiasis, and squamous cell carcinoma.[38]

Demonstration of Donovan bodies in smear or biopsy (Giemsa or silver stain) is the most rapid and specific diagnostic method.[39] Histology reveals pseudoepitheliomatous epidermis and plasmacytic infiltrate with neutrophilic abscesses; cultures are difficult, and PCR is limited to reference laboratories.[14,36,39]

The treatment currently recommended based on guidelines is with antibiotics ≥ 3 weeks or until complete healing[39], with the following antibiotics:

- Azithromycin 1 g PO weekly / 500 mg PO every 24 hours
- Doxycycline 100 mg PO every 12 hours
- Trimethoprim-sulfamethoxazole 160/800 mg PO every 12 hours
- Erythromycin 500 mg PO every 6 hours
- Gentamicin 1 mg/kg IV every 8 h (adjuvant in refractory cases)

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1.	**Genital/perigenital**
	1.1 Ulcerative (Hypertrophic or flat edges)
	1.2 Ulcerovegetative
	1.3 Vegetative
	1.4 Elephantiasis
2.	**Extragenital**
3.	**Systemic**

Table 1. Jardim Classification.[12]

In pregnant women, erythromycin or azithromycin is preferred.[14,36,39] Our case responded to doxycycline with complete cure in six weeks.

Conclusion

Donovanosis is a rare ulcerative infection caused by the intracellular Gram-negative bacillus *Klebsiella granulomatis*.[14] Outside the "hot spots" of Oceania, Africa and India, only scattered series have been described in South America (Argentina, Peru, Brazil and Paraguay) and there is no Mexican case documented in the indexed literature to date.[22,23,24,25,26]

Our patient illustrates several relevant clinical lessons:

1. Extragenital abdominal presentation: although less than 6% of cases are located outside the genital area,[36] these atypical forms should be included in the differential diagnosis of chronic abdominal ulcers.
2. Value of the repeat biopsy: The first sample was nonspecific; the second, targeting active tissue, identified Donovan bodies and established a definitive diagnosis.[39]
3. Screening for immunosuppression and HIV coinfection: Bleeding ulceration increases the risk of viral transmission, so serology should be systematic.[30]
4. Prolonged treatment until healing: doxycycline administered for six weeks achieved complete resolution, in accordance with international guidelines.[14,36]
5. Risk: (Although low) of squamous cell carcinoma in long-standing lesions; any plaque that does not respond to antibiotics requires a repeat biopsy.[31,32,33]

In summary, timely recognition of donovanosis, even in non-endemic areas, depends on maintaining a high level of suspicion for atypical chronic ulcers, confirming the diagnosis with characteristic histology, and applying the appropriate antibiotic regimen until complete healing. Reporting these cases expands regional epidemiological knowledge and reinforces the need for clinical surveillance to prevent serious complications.

Conflicts of interests

The authors have no conflicts of interests.

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