2010 European guideline on donovanosis

Nigel O'Farrell MD FRCP
Ealing Hospital, London, UK.

Guideline editor
Prof. Harald Moi, MD PhD, Section of STI, Department of infectious diseases, dermatology and rheumatology, Oslo University Hospital, and Faculty of Medicine, University of Oslo, Norway

Date: 1st June 2010
Proposed date of revision: June 2015

Adress for correspondence:
Dr. Nigel O'Farrell, Pasteur Suite, Ealing Hospital, Uxbridge road, London UB1 3HW, UK
nigel.o'farrell@eht.nhs.uk

Introduction

The causative organism is *Calymmatobacterium granulomatis*. However, based on evidence of phylogenetic similarity with *Klebsiella sp*, a proposal has been put forward that the organism be reclassified as *K.granulomatis comb nov* though this is debated [1,2]. The organism is a Gram negative facultative aerobe.

The condition has been known under many terminologies other than donovanosis including granuloma inguinale and granuloma venereum. The prevalence of donovanosis has decreased markedly in recent times and the condition can now almost be classified as a sporadic disease. Cases are still reported from Papua New Guinea, South Africa, India, Brazil and Australia although the condition has virtually been eliminated in the latter [3].

DIAGNOSIS

Clinical diagnosis

The incubation period is about 50 days. Papules develop into ulcers that gradually increase in size. Four types of lesions are described [4].

1) Ulcerogranulomatous- the most common type with beefy red ulcers that bleed to the touch.
2) Hypertrophic- usually with a raised irregular edge,
3) Necrotic- offensive smelling ulcer causing tissue destruction,
4) Sclerotic or cicatricial with fibrous or scar tissue

The genitals are affected in 90% of cases and the inguinal region in 10%. Cervical lesions are rare but may mimic carcinoma. Extragenital lesions occur in 6% of cases. Lymph gland enlargement is uncommon. Disseminated donovanosis is rare but secondary spread to liver and bone may occur. As a cause of genital ulceration that bleeds readily, the risk of associated HIV infection is increased and HIV testing and counselling should be considered for all cases [5].

Laboratory diagnosis

Direct microscopy: This is the quickest and most reliable method. A rapid Giemsa method can be used to stain tissue smears that should be prepared by rolling a swab firmly across lesions and rolling this swab evenly across a glass slide to deposit ulcer material [6]. Characteristically there are large mononuclear cells with intra-cytoplasmic cysts filled with deeply stained Gram negative Donovan bodies. Other stains used include Giemsa, Leishman and Wright's. Previous use of antibiotics makes the definitive diagnosis of donovanosis difficult [7].

Histologic examination for Donovan bodies is best done using Giemsa or Silver stains. The characteristic picture shows chronic inflammation with infiltration of plasma cells and polymorphonuclear leucocytes.

Culture: This has only been accomplished in two laboratories in recent times and is not available routinely [8, 9].

PCR: PCR methods have been used including a colorimetric detection method [10, 11]. A genital ulcer disease multiplex PCR test has been developed using an in-house nucleic acid amplification technique that uses *C. granulomatis* primers [12].However, no commercial PCR tests for donovanosis are available currently.

Serology: Serologic tests have been developed but are not reliable

If no diagnostic tools are immediately available, a dry swab should be taken and refrigerated while arrangements for PCR testing are made.

MANAGEMENT

Therapy

Azithromycin 1 g weekly or 500mg daily (Grade B, Level 1b) [13]. Recommended as first-line therapy.
Co-trimoxazole 160/800mg bd (Grade B, Level IIb) [14]
Doxycycline 100mg bd, (Grade C, Level IV) [15] (Trials have not been done but older tetracyclines have been shown to be effective)
Erythromycin 500mg 4 times daily. Recommended in pregnancy (Grade C, Level IV) [16]

Gentamicin 1 MG/Kg every 8 hours can also be used as an adjunct if lesions are slow to respond (Grade C, Level III) [17]

Children with donovanosis should receive a short course of azithromycin 20mg/kg (C IV). Children born to mothers with donovanosis should receive prophylaxis with a 3-day course of azithromycin 20/kg once daily(Grade C, Level IV) [18].

Duration of treatment should be until complete healing is achieved.

Information, explanation and advice for the patient

Patients with donovanosis are often embarrassed or ashamed and reassurance that they have a treatable condition is important, as is the need to take antibiotics until complete healing has been achieved. Tests for HIV and syphilis are recommended.

Partner notification

Donovanosis is uncommon in partners of index cases but sexual contacts in the last six months should still be checked for possible lesions by clinical examination.

Proposed guideline review date: 2015

References

1. Carter J, Bowden FJ, Bastian I et al. Phylogenetic evidence for reclassification of *Calymmatobacterium granulomatis* as *Klebsiella granulomatis comb nov*. *Int J Syst Bacteriol* 1999;**49**:1695-1700

2. Kharsany AB, Hoosen AA, Kiepala P et al. Phylogenetic analysis of *Calymmatobacterium granulomatis* based on 16S sequences. *J Med Microbiol* 1999;**48**:841-7

3. Bowden FJ. Donovanosis in Australia: going, going… *Sex Trans Inf* 2005;**81**:365-6

4. Rajam RV, Rangiah PN. Donovanosis. WHO. Monograph series no 24. Geneva 1954

5. O'Farrell N, Windsor I, Becker P. Risk factors for HIV-1 in heterosexual attenders at a sexually transmitted diseases clinic in Durban. *S Afr Med J* 1991;**80**:17-20

6. O'Farrell N. A rapid staining technique for the diagnosis of granuloma inguinale (donovanosis). *Genitourin Med* 1990;**66**:200- 201

7. Velho PE, de Souza EM, Belda W. Donovanosis. *Braz J Infect Dis* 2008;**12**:521-5

8. Kharsany AB, Hoosen AA, Kiepala P et al. Growth and cultural characteristics of *Calymmatobacterium granulomatis*: the aetiological agent of granuloma inguinale (donovanosis). *J Med Microbiol* 1997;**46**:579-85

9. Carter J, Hutton S, Sriprakash KS et al. Culture of the causative organism for donovanosis (*Calymmatobacterium granulomatis*) in Hep-2 cells. *J Clin Micro* 1997;**35**:2915-7

10. Bastian I, Bowden FJ. Amplification of Klebsiella-like sequences from biopsy samples from patients with donovanosis. *Clin Infect Dis*1996;**23**: 1328-30

11. Carter JS, Kemp DJ. A colorimetric detection system for *Calymmatobacterium granulomatis*. *Sex Transm Inf* 2000;**76**:134-6

12. Mackay IM, Harnett G, Jeoffreys N et al. Detection and discrimination of herpes simplex viruses, *Haemophilus ducreyi*, *Treponema pallidum*, and *Calymmatobacterium (Klebsiella) granulomatis* from genital ulcers. *Clin Infect Dis* 2006;**42**:1431-8

13. Bowden FJ, Mein J, Plunkett C, Bastian I. Pilot study of azithromycin in the treatment of genital donovanosis. *Genitourin Med* 1994;**72**:17-19

14. Lal S, Garg BR. Further evidence of the efficacy of co-trimoxazole in donovanosis. *Br J Vener Dis* 1980;**56**:412-3

15. Greenblatt RB, Barfield WE, Dienst RB et al. Terramycin in the treatment of granuloma inguinale. *J Vener Dis Inf* 1951;**32**:113-5

16. Robinson HM, Cohen MM. Treatment of granuloma inguinale with erythromycin. *J Invest Dermatol* 1953;**20**:407-9.

17. Maddocks I, Anders EM, Dennis E. Donovanosis in Papua New Guinea. *Br J Vener Dis* 1976;**52**: 190-6

18. Bowden FJ et al. Donovanosis causing cervical lymphadenopathy in a five-month old boy. *Paed Infect Dis J* 2000;**19**:167-9

Declarations of interest

Nigel O'Farrell: none
Harald Moi: none

Appendix 1

Search Strategy

A Medline search using the terms donovanosis and granuloma inguinale between 1950-2009 was undertaken
Review of STI guidelines published by the US Centres for Disease Control and UK National Guidelines (www.bashh.org)

Appendix 2

Levels of evidence and grading of recommendations

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomised controlled trials.

Ib Evidence obtained from at least one randomised controlled trial.

IIa Evidence obtained from at least one well designed study without randomisation.

IIb Evidence obtained from at least one other type of well designed quasi-experimental study.

III Evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies, and case control studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grading of Recommendations

A (Evidence levels Ia, Ib)

Requires at least one randomised control trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

B (Evidence levels IIa, IIb, III)

Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

C (Evidence IV)

Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.