GUIDELINE

European guideline for the management of donovanosis, 2010

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Summary: Donovanosis is a rare sexually transmitted infection now mainly seen in sporadic cases in Papua New Guinea, South Africa, India, Brazil and Australia. The causative organism is *Calymmatobacterium granulomatis* though a proposal has been put forward that the organism be reclassified as *Klebsiella granulomatis* comb. nov. The incubation period is approximately 50 days with genital papules developing into ulcers that increase in size. Four types of lesions are described – ulcerogranulomatous, hypertrophic, necrotic and sclerotic. The diagnosis is usually confirmed by microscopic identification of characteristic Donovan bodies on stained tissue smears. More recently, polymerase chain reaction (PCR) methods have been developed. The recommended treatment is azithromycin 1 g weekly until complete healing is achieved.

Keywords: donovanosis, granuloma inguinale, *Calymmatobacterium granulomatis*, genital ulcer disease

INTRODUCTION

The causative organism is *Calymmatobacterium granulomatis*. However, based on the evidence of phylogenetic similarity with *Klebsiella* sp., a proposal has been put forward that the organism be reclassified as *Klebsiella 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 in 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 approximately 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 as may longstanding penile lesions. Extragenital lesions occur in 6% of cases. Lymph gland enlargement is uncommon. Disseminated donovanosis is rare but secondary spread to the 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]

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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 intracytoplasmic 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]

Histological 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 leukocytes.

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

Polymerase chain reaction: polymerase chain reaction (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: serological 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.

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MANAGEMENT

Therapy

Azithromycin: 1 g weekly or 500 mg daily (Grade B, Level 1b).[13] Recommended as first-line therapy

Co-trimoxazole: 160/800 mg twice daily (Grade B, Level IIb)[14]

Doxycycline: 100 mg twice daily (Grade C, Level IV)[15] (trials have not been done but older tetracyclines have been shown to be effective)

Erythromycin: 500 mg four times daily. Recommended in pregnancy (Grade C, Level IV).[16] However, azithromycin is now probably the drug of choice in pregnant women

Gentamicin: 1 mg/kg every eight 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 20 mg/kg (C IV). Children born to mothers with donovanosis should receive prophylaxis with a three-day course of azithromycin 20/kg once daily (Grade C, Level IV).[18]

Duration of treatment should be until complete healing is achieved. If lesions have not resolved by six weeks, biopsy should be performed to exclude carcinoma.

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.

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APPENDIX A

Search strategy

A Medline search using the terms 'donovanosis' and 'granuloma inguinale' between 1950 and 2009 was undertaken.

Review of STI guidelines published by the US Centres for Disease Control and UK National Guidelines (www.bashh.org).

APPENDIX B

Levels of evidence and grading of recommendations

Levels of evidence

Ia Evidence obtained from meta-analysis of randomized controlled trials;
Ib Evidence obtained from at least one randomized controlled trial;
IIa Evidence obtained from at least one well-designed study without randomization;
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 randomized 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 randomized 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.