Tropical STIs

Nigel O'Farrell

What's new ?

- The global burden of chancroid and donovanosis has decreased significantly, but genital herpes has increased
- An outbreak of lymphogranuloma venereum characterized by signs and symptoms of proctolitis is under way in Northen Europe and North America, in men who have sex with men

Genital ulceration is recognized as a significant risk factor for the acquisition and transmission of HIV in heterosexuals in developing countries. This link with HIV has led to renewed interest in the tropical causes of genital ulceration – chancroid, lymphogranuloma venereum (LGV) and donovanosis. In most settings where these conditions are prevalent, few confirmatory diagnostic tests are available. The WHO has therefore recommended that the syndromic approach (see below) be used to manage these patients. Improved public health control of all causes of genital ulceration should be a priority in countries where HIV and genital ulcers are prevalent. This now appears to be happening; the incidence of these conditions has decreased considerably over the last 10 years, though, paradoxically, genital herpes has increased.

Chancroid

Chancroid is an STI causing painful genital sores and inguinal lymphadenopathy that may progress to abscess (bubo) formation. The causative organism is a Gram-negative bacterium, *Haemophilus ducreyi*.

Epidemiology – chancroid is still endemic in many developing countries. The highest prevalences are reported in southern Africa. Small outbreaks have been reported in the USA. Chancroid is associated with prostitution, poor standards of genital hygiene and low socioeconomic status. Asymptomatic carriage of *H. ducreyi* has been reported in female sex-workers.

Pathogenesis – abrasions are necessary for *H. ducreyi* to penetrate the epidermis and cause infection. The organisms are found in macrophages and neutrophils, and free in the interstitium.

Clinical features – the incubation period of chancroid is usually 4–7 days. Lesions usually start as a tender papule that develops into a pustule and then an ulcer. Vesicles are not seen. The classical ulcer has a ragged, undermined edge with a grey or yellow base that bleeds when touched. Lesions may be single or multiple (Figure 1). The usual sites of infection are the prepuce, coronal sulcus, frenulum and glans in men, and the labia minora and fourchette in women. Ulcers of the vaginal wall and cervix may occur. Extragenital lesions are rare. In men, lesions are associated with absence of circumcision.

Painful unilateral or bilateral enlargement of the inguinal lymph glands is common. Buboes may require aspiration.

Sequelae include phimosis and phagedenic ulceration (Figure 2) causing tissue destruction following secondary infection. Buboes that rupture may take a long time to heal.

Diagnosis – nucleic acid amplification tests (NAATs) are now the most sensitive method for diagnosing *H. ducreyi*, but their availability remains limited. Primers have been developed to amplify sequences from the *H. ducreyi* 16S ribosomal RNA gene, the rrs (16S)–rrl (23S) ribosomal intergenic spacer region and the *groEL* gene. Antigen detection using fluorescent techniques may be useful, but is expensive. Serological tests are unable to distinguish between old and new infections.

Culture was the usual method of diagnosis of chancroid, but has been overtaken by NAATs. Culture media must be fresh and may need fine adjustment, depending on the characteristics of local strains of *H. ducreyi*. Two culture media are required to achieve reasonable sensitivity. Media used include gonococcal agar base and Muller Hinton, with various additives and supplements. Thioglycolate hemin-based transport medium may allow storage of viable organisms at 4°C for 24 hours or possibly longer. Most strains are β-lactamase producers. Gram-staining of material from ulcers may show characteristic Gram-negative coccobacilli in a 'school of fish' or 'railroad track' appearance.

Histology shows superficial necrosis with large numbers of neutrophils, endothelial proliferation and infiltration with plasma cells, lymphocytes and fibroblasts.

1 Multiple ulcers of chancroid on the coronal sulcus. (By courtesy of O P Arya.)

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2 Phagedenic chancroid ulceration.

Differential diagnoses include genital herpes, syphilis, donovanosis and LGV. Mixed infections with other causes of genital ulceration should always be suspected.

Management – treatment of chancroid comprises one of the following:

- ciprofloxacin, 500 mg b.d. for 3 days
- erythromycin, 500 mg t.d.s. for 7 days (in pregnant women)
- azithromycin, 1 g stat
- ceftriaxone, 250 mg i.m. stat.

Co-trimoxazole is no longer recommended.

Healing of ulcers is usually achieved after 7–14 days. Longer courses of treatment are sometimes required in HIV-positive patients, who should be followed-up until healing is complete.

Prevention – sexual contacts of index cases should be offered epidemiological treatment. Uncircumcised men should ensure adequate genital hygiene.

Donovanosis (granuloma inguinale)

Donovanosis is a chronic, progressive bacterial infection that usually involves the genital region. The causative organism has been reclassified as *Klebsiella granulomatis comb nov* based on phylogenetic analysis, though there is debate about this; some authorities consider the original nomenclature, *Calymmatobacterium granulomatis*, to be more appropriate.

Epidemiology – donovanosis is endemic in Papua New Guinea, parts of southern Africa and India, and Brazil. A programme targeting aboriginal communities has succeeded in almost eliminating the condition in Australia. Donovanosis is associated with poor hygiene, and is more common in lower socioeconomic groups and in men compared with women.

Pathogenesis – lesions start as a papule or subcutaneous nodule that later ulcerates after trauma.

Clinical features – the incubation period is about 50 days. The classical lesion (ulcerogranulomatous, Figure 3) is a beefy, red ulcer that bleeds readily to the touch. Other types include hypertrophic, necrotic (Figure 4) and sclerotic (uncommon) variants.

The genitals are affected in 90% of patients and the inguinal region (Figure 5) in 10%. The common sites of infection are the prepuce, coronal sulcus, frenum and glans in men, and the labia minora and fourchette in women. In men, lesions are associated with absence of circumcision.

Extragenital lesions may involve the lip, gums, cheek, palate, pharynx, larynx and chest, and the number of case reports of these is increasing. Haematogenous spread to liver and bone is reported. Lymphadenitis is uncommon. During pregnancy, lesions tend to develop more quickly and respond more slowly to treatment.

Complications include carcinoma, pseudo-elephantiasis and stenosis of the urethra, vagina or anus.

Diagnosis – a clinical diagnosis of donovanosis made by an experienced practitioner is usually of high positive predictive value. The diagnosis is confirmed by microscopic identification of Donovan bodies (Figure 6) in tissue smears. Preparation of a good-quality smear is important. A swab should be rolled firmly over an ulcer previously cleaned with a dry swab to remove debris. Smears can be examined in a clinic setting by direct microscopy using a rapid Giemsa or Wright's stain. Alternatively, a piece of granulation tissue crushed and spread between two slides can be used. Donovan bodies can be seen in large, mononuclear cells as Gram-negative, intracytoplasmic cysts filled with deeply-staining bodies that may have a safety-pin appearance.

Histological changes include chronic inflammation with infiltration of plasma cells and neutrophils. Epithelial changes include ulceration, microabscesses and elongation of the rete ridges.

Culture of the organism has been reported in peripheral blood monocytes and in Hep-2 cells. Polymerase chain reaction analysis using a colorimetric detection system can now be used in routine diagnostic laboratories. Serological tests have poor specificity.

Differential diagnoses include syphilis, chancroid, LGV, genital herpes, neoplasm and amoebiasis. Mixed infections are common.

3 Typical lesions of subpreputial ulcerogranulomatous donovanosis.

4 Deep necrotic donovanosis ulcer causing tissue destruction.