Granuloma inguinale, which is considered to be a venereal infection, is characterized by a chronic superficial destructive granulomatous painful lesion with a typically beefy-red appearance involving the genitalia and adjacent tissue. It is caused by Calymmatobacterium granulomatis, previously known as Donovania granulomatis, a Gram-negative bacterium.

First described by McLeod in India 100 years ago, the disease has a world-wide distribution but is more prevalent in tropical and subtropical areas than in temperate and more highly developed countries. Cases are rarely reported from the USA or Western Europe, but are common in the islands of the Caribbean, in India and in New Guinea.

Although Ribeiro notes that the disease is endemic in South Africa, few cases have been reported. These include 2 male patients, 1 in Soweto and 1 a mineworker, and 8 female patients. Our experience in Shongwe Hospital suggests that the disease may be more prevalent than was previously recognized.

Background

Shongwe Hospital, situated in the Nkomazi region of Kangwane in the Eastern Transvaal, serves a population of 150000 people, mainly Swazis. This homeland borders on Mozambique in the east, Swaziland in the south and the area adjoining the Kruger National Park in the north. The climate of the region is subtropical. The population live in semirural conditions in villages and derive their income from cattle ranching and small business establishments. Many earn their living by working in the adjoining intensive farming areas and in industries. A large proportion of the active adult males are migrant workers.

Patients and methods

All the patients described in this report first presented to the Outpatients Department of the Shongwe Hospital. When the condition was diagnosed on clinical grounds as granuloma inguinale the patient was referred to the laboratory for confirmation.

Scrapings were taken from the surface of the granulomatous lesions and films made on clean glass slides. These were air-dried without fixative and stained with a 1 : 10 dilution of Giemsa stain in distilled water for 20 minutes. The stained films were examined microscopically under an oil-immersion objective. The finding of pleomorphic intracellular bacilli with rounded ends and a clear halo (Donovan bodies) was regarded as diagnostic of the infection. It was noted that the organisms stained poorly with Gram’s stain (Fig. 1).

Results

In the period from 1 September 1975 to 30 November 1977, 30 cases of granuloma inguinale were diagnosed and in the period from 1 June 1981 to 15 September 1983 a further 13 cases were recorded. The ages of these patients ranged from 6 to 41 years. Except for a 6-year-old girl all the patients were 18 years or older. The 6-year-old girl had had sexual contact with an older man. The male/female ratio was 27 : 16 and site of the lesion was as follows: labia I, vagina I, vulva 8, penis 21, inguinal region 3, unknown 9.

The serological tests were of some interest in that the Wassermann reaction in the first 5 patients was negative, and
in 4 of them the chlamydial complement fixation tests gave 2 negative results, 1 indeterminate result and 1 positive result.

Treatment was with tetracycline 500 mg 6-hourly for 2 - 4 weeks. In one case erythromycin 500 mg 6-hourly was given for 21 days. However, the relapse rate was high, and treatment with tetracycline had to be repeated, in some cases several times, over a period of months.

The outpatient records for 3 patients could not be traced, and particulars were obtained from laboratory records.

Discussion

Except for the 6-year-girl, who had had sexual contact with an older man, all these patients were in the sexually most active period. The disease is said to be more common in women than in men, but in our series the ratio was reversed, possibly reflecting an underdiagnosis in female patients, in whom the lesions may not be readily detected.

It was not possible to assess the incubation period in our patients, but it has been estimated to be from 8 to 80 days, the average being 34 - 50 days. Examples of the three types of clinical presentation of the disease were seen in our patients. The lesions, which first appear on the genitalia, groin or perineum, may first present as exuberant hypertrophic granulation tissue, soft and velvety to the touch with rolled edges, and never undermined. These lesions have a typical beefy-red appearance suggesting a fleshy mass herniating through the skin. Secondly, the lesions may be ulcerative and covered by foul-smelling membranous exudate with a peculiar acrid smell. On microscopic examination these lesions are secondarily infected, particularly by Vincent’s spirochaetes. Thirdly, cicatricial lesions may develop since a keloid scar remains after healing.

As noted in our patients there is little systemic effect and no regional lymphadenopathy. Untreated granuloma inguinale pursues an indolent relapsing course. Even after treatment relapses may occur, as was evident in our patients. An atrophic scar remains after healing.

Complications include secondary infection, sometimes with phagedenic ulceration and mutilation, which may result in amputation of some parts of the genitalia. Massive cicatrization of the dermis and subcutis — which occurs in 15 - 20% of cases — may cause lymphatic blockage resulting in genital elephantiasis, more frequently seen in female than male patients. The disease has been reported to predispose to carcinoma of the vulva, but this association remains controversial.

The causative organism, *C. granulomatis*, is a pleomorphic non-spore-forming Gram-negative organism sharing antigens with the Enterobacteriaceae, suggesting that it occurs as part of the bowel bacterial flora and that auto-inoculation into sites of trauma may result in clinical disease. In keeping with this hypothesis is the fact that the organism requires certain peptide-like growth factors and anaerobic or micro-aerophilic conditions for its growth. Growth occurs in liquid media and the yolk sac of embryonated eggs. These organisms, occurring singly or in short chains, fail to produce lesions in experimental animals and a similar disease has not been found in animals. The intracellular organisms, together with the presence of antibodies which are not protective, suggests that cell-mediated immunity may be important in the defence mechanisms of this disease. *C. granulomatis* occurs intracellularly in large mononuclear cells. The appearance of these cells is so typical as to be of diagnostic value and may be observed on histological examination of biopsy specimens from the lesions. Serological tests are of some value in detecting antibodies but are of low specificity and are not routinely available.

In treatment the drug of choice is tetracycline, and this was administered to our patients. However, several relapsed and required further courses of treatment. Alternative therapies include chloramphenicol 2 - 3 g/d in divided doses for 10 days, erythromycin 500 mg 6-hourly for a prolonged period, or streptomycin 4 g/d given by intramuscular injection for 5 days. Gentamicin and co-trimoxazole have also been used effectively. In pregnant patients combinations of erythromycin and lincomycin or erythromycin and ampicillin have been used with good results. The disease does not respond to treatment with sulphonamides alone or with the penicillins.

It is important to follow the patient's progress for prolonged periods. In our series relapses occurred months or even years after seemingly effective treatment. In such cases repeat courses of treatment are necessary. Longstanding mutilating lesions and scarring may require surgical repair.

It must be emphasized that genital ulceration may be due to granuloma inguinale as well as to syphilis, chancroid or lymphogranuloma venereum. Differentiation between these conditions is usually possible on clinical grounds. The primary chancre of syphilis is hard with a clearly defined edge and is associated with enlarged firm inguinal nodes, while the lesions of granuloma inguinale have an exuberant beefy-red appearance with no enlargement of the regional nodes; inguinal swellings are pseudobuboes. The primary lesion of lymphogranuloma venereum due to *Chlamydia trachomatis* serovars L1, L2, and L3 is a small evanescent ulcer, often not seen, and the characteristic feature is involvement and enlargement of the regional lymph nodes which, if the infection is not treated, break down and suppurate. This may discharge externally with the formation of fistulas. Chancroid caused by *Haemophilus ducreyi* is characterized by a prominent ulcer with a ragged undermined edge and enlargement of the regional lymph nodes which, if not treated also break down to form a bubo.

The clinical diagnosis of these infections may be confirmed with a high degree of accuracy in the laboratory. *Treponema pallidum* may be demonstrated readily on microscopic examination with dark-ground illumination in scrapings from the chancre. In later stages the serum gives a strongly positive reaction in the Wassermann test, which may be confirmed by the use of other more specific serological tests. The diagnosis of lymphogranuloma venereum may be confirmed by culture of the chlamydiae in egg yolk sac culture or by special tissue culture methods. However, in routine practice the diagnosis is usually confirmed by the results of serological tests, either the complement fixation test or the fluorescent antibody test. In patients with chancroid, the diagnosis may be confirmed by finding Gram-negative bacilli with a 'fish in the stream' appearance on direct examination of films made from the ulcer and by culture on special media of *H. ducreyi*. In cases of granuloma inguinale the diagnosis is established by finding the characteristic Donovan bodies, pleomorphic bacilli with rounded ends, in the mononuclear cells on microscopic examination of films stained with Giemsa stain.

Conclusions

A history of chronicity or recurrence of the genital lesions should alert the clinician to the possibility that his patient has granuloma inguinale. The simple procedure of examining a Giemsa-stained smear can save the patient the humiliation of having to go from clinic to clinic or doctor to doctor to seek help and preserve the mutilation which accompanies this destructive disease. An early diagnosis also enables the correct choice of treatment to be made and its success encourages the patient to come for follow-up treatment until the lesions are healed. In some cases hospital admission is necessary for supervision of the treatment and in other cases for surgical repair.
In view of the increasing incidence of the sexually transmitted diseases we wish to alert the clinician in the field to look for this disease, which we believe is more frequent in South Africa than previously recognized.

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REFERENCES

Comparison of impedance plethysmography with ascending venography for the diagnosis of proximal deep-vein thrombosis

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Summary
In a series of 56 patients with proximal lower-limb deep-vein thrombosis (DVT) diagnosed on ascending venography, impedance plethysmography (IPG) and Doppler ultrasound examinations were performed and the results compared. Both IPG and Doppler ultrasonography were highly sensitive for the diagnosis of proximal occlusive DVT, but considerably less sensitive for the potentially more dangerous proximal non-occlusive thrombosis. If, in the presence of clinically suspected DVT, these non-invasive investigations are both negative, ascending venography remains essential.


The accurate diagnosis of pulmonary embolism (PE) and of the presence and location of deep-vein thrombosis (DVT) is essential before starting anticoagulant therapy if the complications of unnecessary anticoagulation are to be avoided, and also for the implementation of optimal therapy.

In venous thrombo-embolic disease, clinical signs are frequently misleading. Of patients with confirmed PE on angiography, 70% have been shown to have lower-limb DVT on venography;1 up to 80% of these have no physical signs in the legs.2 Furthermore, several studies have shown that the clinical diagnosis of DVT is inaccurate in up to 45% of patients,3 particularly in patients with signs limited to the calf.4

The reference standard for the diagnosis of DVT remains bilateral ascending venography utilizing the now well-established method described by Rabinov and Paulin.5 Although in experienced hands this is safe, quick, accurate and relatively acceptable to patients, it is not without morbidity, and a well-equipped radiology unit is required in order to achieve optimal diagnostic standards.

The invasive nature of ascending venography and its potential complications (pain, anaphylaxis, aggravation or initiation of venous thrombosis) have discouraged its universal acceptance despite the obvious need for accurate diagnosis.

Impedance plethysmography (IPG), which is non-invasive and simple to perform, is rapidly gaining favour as a method of diagnosing popliteal or more proximal DVT.6,7 calf vein thrombosis, unless extensive, cannot be reliably detected by IPG alone. However, its use in combination with 125I-fibrinogen scanning is claimed to provide diagnostic sensitivity and specificity in excess of 92% (compared with venography) for both calf vein and proximal thrombosis.8,9 A disadvantage is that the fibrinogen scan takes up to 3 days and is usually available only in the restricted environment of a teaching hospital.

In this article we present the results of a comparison between IPG and bilateral ascending venography in the diagnosis of proximal DVT in 56 patients with venographically proven proximal thrombus.