Primary endometrial and endocervical granuloma inguinale (donovanosis)

Case report

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SUMMARY Primary endometrial and endocervical granuloma inguinale (donovanosis) was diagnosed in an 18-year-old Melanesian woman in Papua New Guinea. Granulomatous involvement of the parametrium, salpinges, ovaries, and ureters was associated with ureteric obstruction and bilateral hydronephrosis. Granuloma inguinale of the cervix, labia majora, and anus developed after diagnostic endometrial curettage. Treatment with tetracycline and later chloramphenicol had to be stopped because of poor patient compliance. Hysterectomy was performed, after which the patient made a good recovery. This appears to be the first case of primary endometrial and endocervical granuloma inguinale to be reported.

Introduction

Granuloma inguinale (donovanosis) is a mildly contagious, chronic, painless, ulcerative disease of the skin and lymphatic systems of the external genitalia, perianal area, and inguinal regions, which is usually transmitted by sexual intercourse. The disease is caused by the Gram-negative bacillus *Calymmatobacterium granulomatis*, which may be detected in large clusters in cyst-like spaces in the cytoplasm of large mononuclear cells in scrapings from lesions. In histopathology reports the organisms are commonly referred to as Donovan bodies. Extracellular bacilli may be observed, and the organism has been recovered from faeces. *C. granulomatis* is best shown by the silver impregnation method but satisfactory definition is obtained with Giesma, Wright's and Leishman's stains and to a lesser extent with haematoxylin and eosin. It grows readily at 37°C in the yolk sac of the chick embryo. In most cases the clinical diagnosis is confirmed by histopathology. In doubtful cases the complement fixation serological test may be of value,¹ though the sensitivity and specificity of the test, which is not commercially available, is low.

The lesions of granuloma inguinale may spread from the external genitalia or perianal area to the

cervix.^{3,4} The uterus, fallopian tubes, and ovaries are rarely affected.³ Primary cervical granuloma inguinale^{3,5} may be associated with involvement of the endometrium⁷ and the uterus, fallopian tubes, and ovaries.⁶ Extragenital lesions may occur in many different sites⁸ by autoinoculation or by spread from genital lesions.³ Haematogenous dissemination with metastatic lesions in bone is a rare complication.⁹⁻¹¹

In the present case cervical ulceration was not visible but endocervical and endometrial granuloma inguinale was present and affected parametrial and pelvic structures; it later spread to the cervix, the labia majora, and the anus.

Case report

An 18-year-old married Melanesian woman from Chimbu Province in the highlands of Papua New Guinea was admitted to Port Moresby General Hospital on 1 June 1981. She had had backache for a year, menorrhagia for several months, and a blood-stained vaginal discharge and polyuria for a month. She had had two uncomplicated pregnancies, the last of which occurred three years before.

CLINICAL FEATURES

On admission she was pale and her temperature was 37.2°C. Ankle oedema was present and a firm, painless suprapubic mass was palpable. The external genitalia and the vagina were normal but the anterior lip of the cervix was slightly distorted and retracted;

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neither cervical erosion nor ulceration was visible. Serosanguinous fluid exuded from the cervical os. The uterus was the size of an 18-week pregnancy and was non-tender and mobile. Because of parametrial induration the adnexae were difficult to define. The anus and perianal region were normal.

INVESTIGATIONS

The urine contained protein 1.5 g/l but no sugar. Microscopy of the centrifuged urine deposit showed a few white cells and white cell casts but bacteria were not isolated in culture. The haemoglobin concentration was 6.4 g/dl and the white blood count $8.7 \times 10^9/l$ with 86% neutrophils; the film showed hypochromic normocytic anaemia. Malarial parasites were not seen. Routine biochemical test results including estimation of the serum creatinine and the fasting and postprandial blood sugar concentrations were within normal limits. The results of the pregnancy test and the Venereal Disease Research Laboratory test were negative as was that of the Mantoux test. The stool contained hookworm and *Trichuris trichura*. Pathogenic microorganisms were not isolated in culture of vaginal material. X-ray examination of the chest showed no abnormality.

CLINICAL COURSE AND TREATMENT

A diagnostic curettage was carried out on 18 June 1981 after a blood transfusion, and endometrial biopsy specimens were obtained. The curettings consisted of caseous material, and endometrial tuberculosis was provisionally diagnosed. Pending the results of histological examination simultaneous treatment with isoniazid and thiacetazone was started together with prednisone 40 mg daily. Ten days later Donovan bodies were found in the endometrial biopsy specimen. Granuloma inguinale was diagnosed and oral tetracycline 500 mg six hourly by mouth given, and the antituberculosis treatment and prednisone stopped. Unfortunately two days later the patient insisted on leaving hospital. She was given a two weeks' supply of tetracycline and was advised to report back to the outpatient department, but she did not do so.

READMISSION

On 23 July 1981 she returned complaining of increased swelling of her ankles, an offensive vaginal discharge, and sores on her vulva and anus. She had failed to complete the course of tetracycline. Examination showed painless enlargement of the uterus and ascites. On vaginal examination five indurated, painless, beefy-red granulomatous ulcers on the labia majora and one each on the cervix and anus were noted. Pelvic examination under anaesthesia showed

multiple indurated masses merging into the enlarged uterus. Biopsy specimens from each of the ulcers contained Donovan bodies. An intravenous pyelogram showed bilateral ureteric obstruction and hydronephrosis. The serum creatinine concentration was 70 $\mu\text{mol/l}$. Initially chloramphenicol 500 mg by mouth every six hours was given. After 14 days' treatment there was no clinical improvement and laparotomy was undertaken.

LAPAROTOMY

At operation the pelvis was found to be invaded extensively by inflammatory granulomatous masses which affected the parametrium, uterine tubes, ovaries, broad ligaments, and ureters. Granulomatous tissue merged with the enlarged uterus, and adhesions of the sigmoid colon, the caecum, and appendix were found. The adhesions were divided and the granulomatous masses excised, after which panhysterectomy and salpingo-oophorectomy were carried out. Postoperatively treatment with chloramphenicol was continued for three weeks, and her convalescence was uneventful. The ulcers on the external genitalia and the anus healed and the hydronephrosis resolved with no further polyuria. She remained well after discharge but failed to return for review at six weeks and could not be traced.

HISTOPATHOLOGY

Endometrial biopsy specimens obtained on 18 June 1981 and those of cervical, vulval, and anal ulcers on 27 July 1981 showed a chronic granulomatous reaction with vacuolated macrophages containing bacilli, which when stained with haematoxylin and eosin were typical of *Calymmatobacterium granulomatis*. When examined on 10 August 1981 the uterus measured 10×4 cm and was covered externally with granulomatous adhesions and large nodules. The endometrium and endocervix appeared normal, but multiple sections stained with haematoxylin and eosin showed a chronic inflammatory reaction and vacuolated macrophages containing Donovan bodies. These last were also evident in large foamy histiocytes throughout the granulomatous nodules in which the salpinges and ovaries were embedded.

Endometrial biopsy specimens were sent to the pathology department at the Royal Brisbane Hospital, Brisbane, Australia, where silver impregnation stains were carried out. This confirmed the presence of *C granulomatis* within the endometrium (figure).

Discussion

Granuloma inguinale occurs in many tropical areas including northern Australia, India, and Guyana and

FIGURE Endometrial biopsy specimen showing (a) the granulomatous reaction in the stroma with foamy macrophages, polymorphonuclear granulocytes, and plasma cells (H & E $\times$ 250); (b) large foamy histiocytes with eccentric nuclei and groups of rod-shaped intracellular Donovan bodies within the cytoplasm (Warthin Starry stain $\times$ 1000).

is also prevalent among Negro homosexuals in the south-eastern states of the United States of America.¹² The disease was probably introduced into Papua New Guinea during the early colonial period.¹³ Subsequently it became one of the most prevalent venereal diseases, occurring especially in young immigrant men in Port Moresby.¹¹ By 1975 it had become the commonest cause of anogenital lesions in women in Port Moresby.¹⁴

In most cases granuloma inguinale is limited to the vulval, inguinal, and perianal regions but may rarely spread to the cervix^{3,4}; it may then resemble carcinoma,¹⁵ as may primary cervical granuloma inguinale itself.^{5,6} Even more unusual are cases in which the disease extends from the external genitalia and cervix (or from a primary cervical lesion) to the uterus and pelvic structures; in these cases it may simulate advanced pelvic cancer.^{6,7,14,16}

In Jofre's case¹⁶ there was extensive involvement of the external genitalia and perianal areas as well as

the cervix, uterus, parametrium, and adnexae, which produced a "frozen pelvis" and simulated pelvic cancer. Total resolution occurred after treatment for 10 weeks with tetracycline in an oral dose of 250 mg four times a day. In the case of primary cervical granuloma inguinale described by Bhagwande et al⁷ there was no visible improvement despite five weeks' treatment with streptomycin. As a coexistent carcinoma may have been present hysterectomy was performed. Histopathology showed extensive endometrial granuloma inguinale. In the case reported by Vacca et al¹⁴ fungating cervical lesions suggesting cervical carcinoma were associated with bilateral parametrial induration extending to the side walls of the pelvis with ureteric obstruction and hydronephrosis. Complete resolution occurred after treatment with chloramphenicol (the duration of treatment was not stated). In the case reported by Pund and Gotcher¹² histopathological examination confirmed that granuloma inguinale had spread from

the cervix to the uterus, tubes, and ovaries. As well as simulating carcinoma of the genitalia granuloma inguinale may be associated with the subsequent development of neoplasia,^{15 17 18} though this has not been established.²

In the present case there were no cervical ulcers or erosions initially, and the infection probably began either in the endometrium, with subsequent spread to the parametrium and endocervix or in the endocervix extending subsequently to the endometrium, the parametrium, and other pelvic structures. In view of the extensive endometrial and pelvic disease and minimal endocervical involvement a primary endometrial focus is probable in this case. The later development of ulcers on the cervix, vulva, and anus may have resulted from abrasion of these areas² during diagnostic curettage and contamination by infected endometrial curettings. Depression of immunity by high doses of prednisone may have contributed to their evolution. The incubation period for granuloma inguinale lesions may vary from a few days to several months.¹⁸

This case indicates that even when there is no visible cervical ulceration endocervical and endometrial granuloma inguinale may be present. Especially in tropical countries where granuloma inguinale is endemic this possibility should be considered in the differential diagnosis of apparent endometrial tuberculosis or advanced pelvic cancer with or without osteolytic bone metastases.

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