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Granuloma inguinale detected during pregnancy: A case report from Northern India

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Abstract

Granuloma inguinale (donovanosis) is a very rare slowly progressive sexually transmitted disease. With the introduction of antibiotics, its incidence has declined dramatically. Very few cases are now reported from countries like New Guinea, KwaZulu-Natal, southern parts of Africa, Brazil and the West Indies. Southern states of India have witnessed few cases of donovanosis in the past few decades. We hereby report a very rare case of granuloma inguinale diagnosed and successfully managed during third trimester of pregnancy and puerperium. However, caesarean delivery had to be done due to presence of ulcero-granulomatous lesion at the vulva with risk of bleeding during vaginal delivery.

Keywords: Granuloma inguinale, donovanosis, granulomatous vulval lesion, genital ulcer, sexually transmitted disease (STD) in pregnancy

Introduction

Granuloma inguinale (donovanosis) is a very rare slowly progressive sexually transmitted disease. With the introduction of antibiotics, its incidence has declined dramatically. Very few cases are now reported from countries like New Guinea, KwaZulu-Natal, southern parts of Africa, Brazil and the West Indies ^[1]. Southern states of India have witnessed few cases of donovanosis in the past few decades. In Puducherry, donovanosis accounted for 14% of genital ulcer cases referred to STI clinics of whom about 15-20% were HIV positive ^[2]. Its incidence had significantly declined in northern India in the 1990s and today it is extremely rare here. We hereby report a very rare case of granuloma inguinale diagnosed and successfully treated during third trimester of pregnancy and puerperium. However, caesarean delivery had to be done due to presence of ulcero-granulomatous lesion at the vulva with risk of bleeding during vaginal delivery.

Case Report

A twenty-two year old primigravida presented at 28 weeks of gestation with complaints of a painful ulcer in the vulva for six months. Noticeable enlargement of the ulcer had occurred over two weeks. Initially she took over the counter analgesics but pain gradually progressed. There was no inguinal lymphadenopathy. Her husband was asymptomatic and worked as a labourer in a factory elsewhere. On careful enquiry, she gave history of multiple sexual partners prior to conception.

Examination of the vulva revealed an ulcero-granulomatous lesion of about 4*4 cm. extending from the posterior fourchette to left labium majus and minus. Based on history, possibility of sexually transmitted disease was most likely. However, considering the long standing nature of the disease, a differential of malignancy was also kept in mind. Dermatology consultation was sought. Punch biopsy was taken and sent for histopathological examination, Gram Stain and Cytomegalo Virus (CMV) IgG and IgM. Microscopic examination of vulval biopsy showed presence of dense granulation tissue and capillary proliferation with few lymphocytes, plasma cells, scattered neutrophils, histiocytic cells and nuclear debris. There was fibrin deposition in vessels. No granuloma. No dysplasia or malignancy was seen. Gram Stain, AFB Stain and PAS stain were negative. A Giemsa stain of the tissue smear was negative for Donovan bodies. On the basis of these reports, differential diagnoses of CMV, amoebiasis and giant chancroid were now considered. Urine for Chlamydia antigen was negative. PCR for Chlamydia and N. Gonorrhoea, TPHA and RPR serological tests for syphilis and ELISA for HIV-1 & 2 were all

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negative. Oral Clindamycin and Metronidazole were administered but there was no relief.

Repeat clinical examination was conducted and possibility of donovanosis was now considered. Antibiotics were accordingly changed to oral Azithromycin 500 mg once weekly for three weeks. Ultrasound and non-stress test for fetal surveillance was normal with a biophysical profile of 10/10. Meanwhile, she developed preterm labour pain at 34 weeks gestation. Dermatology opinion was sought for deciding the mode of delivery. Considering the presence of ulcero-granulomatous and sloughed-out wound at the vulva and risk of excessive haemorrhage from ulcer during the process of vaginal delivery, decision was taken to conduct abdominal delivery. Caesarean was performed and a live born baby girl of 2.4 kg was delivered. Intra-op and post-op period were uneventful. She was discharged at third day post caesarean with the advice to continue oral azithromycin 500mg once weekly. Genital ulcer improved drastically after 2 doses of Azithromycin thereby confirming the diagnosis of Granuloma inguinale. Presently, there is no residual skin lesion seen at the vulva.

Discussion

Donovanosis, a chronic cause of genital ulceration, is extremely rare in northern part of India. The causative organism, *Calymmatobacterium granulomatis*, can be cultured after polymerase chain reaction from representative skin biopsies from involved areas. Phylogenetic analysis has shown close similarity with the genus *Klebsiella* and so it has been recently reclassified as *Klebsiella granulomatis*. It is characterised by specific genital ulcers. These ulcers being painless, often get mistaken for syphilis. Thus they remain untreated for long and progress to destroy internal tissues and genital organs. These ulcers are often the harbouring sites for other bacterial superinfections. Symptom starts with the appearance of small painless nodular lesions in the contact areas after an incubation period of 10 to 40 days. Later, these nodules burst open creating ulcers with fleshy, oozing lesions. Tissue destruction and mutilation may continue to progress until antibiotics are timely started. Recently, azithromycin has emerged as the drug of choice in suspected and diagnosed cases of donovanosis [2, 3]. Syndromic management protocols for genital ulceration may be adopted locally for donovanosis in endemic countries like Durban where an epidemic was reported in 1997-98 [4]. Relative paucity of interest in the disease by health care professionals has led to inadequate treatment and elimination in most countries. Marked contrast was observed in Australia where a proactive approach was launched in 1990s leading to successful elimination of the disease from the continent [2].

Donovanosis tends to be more prevalent in populations that are impoverished, marginalised and with limited access to safe sanitary and sexual practices. Although primarily considered as an STI, literature review by Carter *et al.* has led to upcoming arguments whether or not to classify it as an STI. Points in favour of STI origin are increased incidence in age groups with highest sexual activity, history of unsafe sexual exposure in most patients before the appearance of lesions, more prevalence in commercial sex workers and anal lesions in homosexual men practising receptive anal intercourse. However, factors like occurrence in children and sexually inactive adolescents, rarity in sexual partners of index cases, unusual sites of primary non-genital lesions and no definite incubation period have led to arguments against STI origin of donovanosis.

Classically 4 types of donovanosis have been described. The commonest type is ulcero-granulomatous which looks beefy-red,

non-tender and bleed readily to touch and become quite extensive if left untreated. The second variety being hypertrophic or verrucous type with dry, irregular edged protruding ulcers. Other rare varieties are the necrotic type with foul smelling deep ulcer and the sclerotic or cicatricial type with fibrous and scar tissue. Genital lesions constitute 94% cases. Extragenital ulcers occur over lips, gums, cheek, pharynx, neck, nose, chest, etc. Dissemination to lungs and bone have also been reported [3]. Diagnosis is based upon physical examination and thorough clinical and sexual history and contact tracing. Classical "beefy-red" ulcers with characteristic rolled edges and granulation tissue aid in prompt diagnosis. The basis difference from syphilis is that inguinal lymphadenopathy is rare here. Presence of Donovan bodies, rod-shaped organisms in the cytoplasm of mononuclear phagocytes and histiocytes in tissue biopsy is almost a confirmatory sign. These Donovan bodies are even better visible with Wright's stain where they appear deep purple in colour.

Donovanosis is very rarely reported in pregnancy. However, its severity tends to increase during pregnancy probably due to altered maternal immunocompetence and lymphocyte proliferative responses in the third trimester [5]. So, clinicians examining antenatal women with atypical genital ulcers should suspect the possibility of donovanosis and start antibiotics at a lower threshold. Vaginal delivery can be allowed in women where the size of ulcer has decreased following treatment. Active cervical or vulvo-vaginal ulcers tend to bleed profusely with perineal stretching during second stage of labour. So, caesarean delivery is a safer mode in these individuals [3]. Like a non-pregnant individual, donovanosis in pregnancy is also treated with timely initiation of Erythromycin or Azithromycin. Thus, almost all countries worldwide have a very low incidence of this STD today. Being a sexually transmitted disease, contact tracing and partner treatment remains the cornerstone of effective treatment protocol. Promotion of condoms and avoidance of multiple sexual partners can go a long way in preventing this disease.

Various antibiotics recommended for the treatment of granuloma inguinale include Azithromycin 1 gram oral weekly for minimum 3 weeks, Erythromycin base 500 mg orally four times daily, doxycycline 100 mg oral twice daily, ciprofloxacin 750 mg oral twice daily, sulfamethoxazole-trimethoprim double strength tablet (800mg/160mg) twice daily, etc. All antibiotic regimens are prescribed for 3 weeks duration. CDC 2015 has recommended Azithromycin weekly dose to be the drug of choice. There is usually good response to antibiotic. Symptoms begin to subside by the end of first week of treatment but adherence to medication is advised for at least three weeks to prevent relapse. Timely diagnosis and prompt treatment is the key to elimination of this highly infectious STD. The true holds for our case also. Had our patient come early to hospital and treatment initiated at initial stage of the disease, ulcer would not have progressed to this stage and vaginal delivery could have been possible. Thus it is recommended that pregnant females be examined carefully so that such identifiable diagnosis not missed in health care setting henceforth. Strict vigilance and larger study need to be conducted to formulate guidelines for initiating treatment for donovanosis in pregnancy.

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