

## Reports on Scientific Meeting

### Social Hygiene Symposium 2002

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#### Evaluation of genital ulcer

Speaker: Dr. K. K. Ho

Genital ulcer is one of the most common presentations of sexually transmitted infections. The common pathogens include herpes simplex virus (HSV), treponema pallidum (primary syphilis or chancre), haemophilus ducreyi (chancroid) and chlamydia trachomatis (lymphogranuloma venereum, LGV). The prevalence of each aetiology varies geographically. Genital herpes is the most common diagnosis in United States and Europe. Chancroid is more prevalent in developing countries such as sub-Saharan Africa. In Hong Kong and China, chancroid is uncommon and LGV is very rare. There are also non-infectious causes of genital ulcers such as fixed drug eruption, erythema multiforme, Bechet's disease, Crohn's disease, neoplasm and trauma.

#### *Genital herpes*

Genital herpes typically presents with recurrent multiple grouped shallow ulcers. More than 80% of genital herpes are caused by HSV type 2 and about 15% by HSV type 1. The presence of multinucleated giant cells in smear supports a

diagnosis of herpes. Viral culture obtained in early vesicular stage remains the gold standard investigation in diagnosis and differentiation of the type of virus. Routine serology by complement fixation technique is unhelpful because there is considerable cross reactivity between HSV-1 and HSV-2. Type specific serology tests have been developed and are used mainly in sero-epidemiology survey, serodiscordance couple and monitoring in late pregnancy. There is limitation in their role in diagnosing primary genital herpes, as a positive type-specific antibody test does not equate to the cause of genital lesion.

#### *Primary syphilis*

Primary chancre is characterized by single solitary painless indurated clean-based ulcer. Associated firm, non-tender inguinal lymph nodes are sometimes found. Dark field examination enables detection of motile spirochaete, treponema pallidum. In suspicious cases, the examination should be done daily for three consecutive days. Although it remains the standard in diagnosis, it requires technical expertise that may not be readily available. The organism cannot be cultured and serology plays an important role in screening. VDRL (Venereal Disease Research Laboratory), FTA-Abs (Fluorescent Treponemal Antibody absorption) and TPHA (treponemal pallidum haemog-glutination) tests are commonly available in Hong Kong. VDRL may sometimes be negative in secondary syphilis due to the prozone phenomenon. Paired serology three months apart is useful in diagnosis.

### *Chancroid*

Chancroid usually presents with multiple painful deep undermined purulent ulcers with unilateral tender lymph nodes. The diagnosis is suggested by tracking of gram-negative rods in mucus strands in a smear taken from the ulcer, giving a 'shoal of fish' appearance under microscopy. Definitive diagnosis is made by the isolation of *haemophilus ducreyi* in haemin-rich culture media.

Multiplex polymerase chain reaction has been developed to detect the above three organisms from a genital ulcer using one single swab. The sensitivity is high and the results can be available in a few hours. The specificity is more than 95% when clinical chancre or chancroid is seen. However, its use is limited by cost and technique. Clinical diagnosis is important in practice. In a recent study in China, about one-third of genital ulcer is due to syphilis and about 12% had concomitant infection of more than one aetiology. The causes remain unclear in almost one-third of cases.

#### ***Learning points:***

*Management of genital ulcer includes accurate diagnosis, appropriate investigations and treatment. Education, contact tracing and HIV counseling and testing are also important.*

### **High-risk human papillomavirus in local high-risk women (STD clinic attendees and HIV-1 positive women)**

Speaker: Dr. W. K. Tang

Over 100 types of human papillomaviruses (HPV) have been identified. Certain types such as type 16, 18, 31, 33, 58 tend to affect the lower genital tracts. These infections are more persistent and possess moderate to high oncogenic potential. Genital wart is the third commonest sexually transmitted infections in Hong Kong according to the Social Hygiene Service statistics in year 2000.

HPV are small DNA viruses containing approximately 7900 base pairs. HPV type 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 82, 83 are considered intermediate to high-risk in causing genital tract malignancy. Their transmission is mainly through sexual contact. Type 6, 11, 40, 42, 53, 54, 57, 66, 84 are of lower oncogenic potential. Type 6 and 11 may cause laryngeal papillomatosis in babies through vertical transmission.

The incubation period of HPV infection varies from one to eight months. Seventy percent of patients have spontaneous remission, with undetectable HPV twelve months after the initial infection and only nine percent have persistent infection after 24 months. The risk factors for persistent infection include HIV-1 infected persons, old age, immunocompromised, multi-type infection. HPV is associated with various degrees of cervical abnormalities including atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL) and squamous cell carcinoma.

The two most important HPV proteins in the pathogenesis of malignant disease are E6 and E7. They bind to protein products of two cellular tumor suppressor genes p53 and retinoblastoma (Rb) respectively. These proteins regulate normal cell division. After binding to E6 and E7, normal cell control is lost leading to immortalization of cell lines. In HIV patients, the tat-1 gene would bind to E2 protein leading to reduction in its inhibitory effect on E6 and E7 and enhances HPV replications.

The presence of koilocytes in cervical smear cytology is suggestive of HPV infection. Diagnosis of HPV can be made by various methods including in-situ hybridisation, southern transfer hybridization, dot blot, and filter hybridisation. Polymerase chain reaction (PCR) is the most sensitive method. Hybrid capture assay is available as commercial kit and is as sensitive but less specific.

A recent surveillance study based on STD clinic attendees and HIV-1 positive women showed that 48.3% were HPV positive (by type-specific PCR for HPV 16, 18, 58 and nucleotide sequencing of the nested PCR products). Twenty-four percent of the participants (majority are not commercial sex worker) had oncogenic types and 12.8% had low-risk HPV and 5.2% had multiple infections. Among HIV-1 infected women, 27.5% were co-infected with oncogenic HPV. The overall prevalence of HPV infection in local STD clinics had increased four folds when compared to data ten years ago. Compared to overseas data, the prevalence in the West is about 20% to 46% in all population. It was estimated to be about 43% in HIV patients and 13% on non-HIV patients. About 14% of commercial sex worker in Singapore is positive for oncogenic type of HPV. The most important risk factor for oncogenic HPV infection is HIV-1 positivity. Other factors including black race, young age, frequency of vaginal sex, alcohol, oral contraceptive pills are less consistently reported.

The role of HPV testing as primary screening test of cervical malignancy in asymptomatic patient is still a debate. It is generally agreed that a combination of Pap's smear and HPV testing is a sensitive method to pick up patients with equivocal cervical smear results, such as ASCUS for further investigations.

***Learning points:***

*Oncogenic HPV is an important cause of anogenital malignancy. It must be ruled out in high-risk women with this infection.*

**Syndromic approach to management of sexually transmitted infections**

Speaker: Dr. K. T. Chan

Effective management of sexually transmitted infections (STIs) is essential in controlling their

spread, which may otherwise have major socioeconomic consequences. Around 50% of STIs remain asymptomatic. Service delivery and management of STIs can be divided into resources rich and resources poor settings. The former emphasized on aetiological approach to STI management that requires quality assured laboratory supports and instantaneous administration of treatment. The World Health Organization advocates STI syndromic management that is a practical, evidence-supported, cost-effective approach to STIs in resources poor settings, such as primary care settings.

Syndromic management requires front-line staff to diagnose and treat STIs at the first visit, recognizing STIs through symptoms and signs. The syndromic approach can provide acceptable, accessible, rapid and effective treatment at first instance without complications. This approach covers the majority of STIs and the most serious diseases. However, the syndromic approach has limitations in management of vaginal discharge and genital ulcers. Vaginal discharge adopted by syndromic approach does not take into account the asymptomatic nature of STI related cervicitis. On the other hand, the sensitivity of diagnosing genital ulcer due to genital herpes or primary syphilis may vary as a result of the difference in the experience of the primary health care physicians. Effective management of STIs reduces their spread in the community, lowers antibiotic resistance as well as HIV incidence rate, but it should be modified according to local health care systems. The main STI syndromes include urethral discharge in men, vaginal discharge in women, genital ulcers, genital growths in men and women, scrotal swelling, lower abdominal pain and conjunctivitis in neonates. The algorithms must take into account the risk assessment profile of local high-risk population, using single dose and combination therapies in addition to health education, harm reduction like condoms promotion and partner notification.

Treatment of urethral discharge should cover gonococcal and chlamydial infections. The first line antibiotics comprise single dose of ceftriaxone 400 mg and doxycycline 100 mg twice daily for one week. Persistent or recurrent urethral discharge usually results from re-infection, poor compliance or antibiotic resistance. One single dose of metronidazole 2 g can be used to cover trichomonas vaginalis after ruling out the above possibilities.

Syphilis and genital herpes account for the majority of genital ulcers. The presence of vesicles and history of recurrence supports the diagnosis of genital herpes. The ulcers of primary syphilis are often larger and of diameter around 1.5 to 2 cm. Other rarer causes include chancroid, lymphogranuloma venereum and granuloma inguinale. Penicillin remains the first line treatment for syphilis.

The management of vaginal discharge depends on the severity of symptoms (such as absence or presence of lower abdominal tenderness) and the risk profile (including age, marital status, new sexual partners in past 3 months, and current partner with STI and condom use). High-risk group should be treated as cervical chlamydial and gonococcal infections. For low-risk group bacterial vaginosis, trichomonas vaginalis and candidiasis may be considered. Lower abdominal pain may be due to pelvic inflammatory disease which can be treated by intramuscular ceftriaxone 1 g every eight hours together with doxycycline 100 mg twice daily and metronidazole 500 mg twice daily. For the above regimens, therapy should be continued until at least two days after the patient has improved and should be continued with either doxycycline 100 mg orally twice daily for 14 days or tetracycline 500 mg orally four times daily for 14 days. Intramuscular spectinomycin can be given if patients are sensitive to beta-lactams.

In managing scrotal swellings, the diagnosis of epididymitis depends on the risk assessment profile, recent venereal exposure and age. The main differential diagnosis is torsion of testis that

warrants an urgent surgical referral. The history of scrotal trauma, previous torsion, elevated and rotated testis help to differentiate between these two conditions.

### ***Learning points:***

*The World Health Organization advocates STI syndromic management that is a practical, evidence-supported, cost-effective approach to STIs in resources poor settings, such as primary care settings.*

## **Geriatric dermatology**

Speaker: Dr. L. S. Ku

### ***Biology of the aging skin***

The epidermis becomes thinner with age and its water binding capacity is reduced. The amount of collagen decreases with age and collagen bundles become fragmented and disoriented. Elastic fibres are progressively reduced and disintegrated. These changes lead to wrinkling and loss of elasticity of elderly skin. Sebum secretion declines with age. The immune function of aging skin also declines, resulting in increased risk of photo-carcinogenesis and skin infections.

### ***Senile pruritus***

This may be localised or generalised. It is crucial to exclude primary cutaneous or systemic causes of pruritus before attributing the symptom to senility. The important causes of pruritus include liver diseases, renal failure, lymphoma, haematological malignancies, thyroid dysfunction and drugs. Candidiasis accounts for the itch in the majority of patients with diabetes mellitus. Management is difficult, comprising administration of emollients, soothing agents, anti-pruritics, topical steroid, and sedating anti-histamines.

### ***Asteatotic eczema***

This common skin condition is often worse in winter and is most pronounced in the lower limbs. The

skin has a cracked appearance and is aggravated by frequent washing and central heating. Emollients improve xerosis and reduce the need of topical steroid. They should be applied immediately after bathing. Hot water bathing and soap are to be avoided. Topical steroids may be used but elderly patients are more prone to the adverse effects.

### *Stasis eczema*

Stasis eczema is common in elderly, especially those with chronic lower limb oedema and varicose veins. It may present with weeping and crusting eczematous lesions mainly on medial aspect of lower limbs. Dry, scaly, hyperpigmented, ulcerative and atrophic changes may be found in chronic stages. The causes include venous insufficiency, minor trauma and allergic reaction to extravasated protein antigens. Treatment consists of correction of varicose veins, emollient, topical steroid, potassium permanganate wet compresses and eradication of infection. Leg elevation and compression stockings are also important.

### *Psoriasis*

Elderly patients tolerate erythrodermic and pustular psoriasis less well than younger patients especially in terms of cardiovascular stress, and they are prone to cardiac events. Moreover, treatment can be more difficult. Firstly, they may be unable to apply topical therapy properly or travel to and from clinics for phototherapy. Secondly, the presence of hyper-lipidaemia, impaired liver and renal functions and potential drug interactions also adversely affect the choice of treatment. Methotrexate is one of the favoured choices in elderly patients. Small doses of methotrexate are well tolerated and keep the disease controlled, but long-term administration is limited by side effects and potential adverse drug interactions.

### *Bullous pemphigoid*

The differential diagnosis in the elderly includes friction blisters, bullous impetigo, pemphigus vulgaris, diabetic bullae, and epidermolysis

bullosa acquisita. Bullous pemphigoid is mainly a disease of elderly over 60 years of age and presents as large tense blisters with erythematous on urticarial bases. It is an autoimmune disease with circulating anti-skin antibodies against the dermo-epidermal junction. Eroded skin from ruptured blisters often showed a good tendency to re-epithelialise and does not scar. Although it is a self-limiting disease, it may last for month or years. Localised disease can be treated with potent topical steroids alone. Extensive disease is usually managed with systemic corticosteroids with or without steroid sparing agents. Adjunctive agents such as tetracyclines may be used.

### *Chronic leg ulcers*

Most chronic leg ulcers are due to venous hypertension. Underlying causes especially venous or arterial insufficiency must be corrected. Daily dressing with antiseptics is necessary but repeated courses of antibiotics without positive culture is not justified. Debridement and skin grafting may be needed in difficult cases.

### *Scabies*

It is caused by *Sarcoptes scabiei* var *hominis* and may mimic senile pruritus. The common sites involved are finger webs, wrists, antecubital fossae, axillae and genitalia. A high index of suspicion is needed and the diagnosis is confirmed by microscopy of skin scrapings of papules or burrows. Treatment includes topical benzyl benzoate, malathion or  $\gamma$ -benzene hexachloride. Crusted (Norwegian) scabies though uncommon is highly contagious. It typically occurs in debilitated or mentally retarded patients often appearing as itchy or non-itchy psoriasiform dermatitis with thick crusts and scales over hands and feet. Vigorous treatment with benzyl benzoate for four days and adequate treatment of contacts are indicated. Oral ivermectin can be considered if topical treatment fails.

### *Herpes zoster*

It is common in the elderly with incidence of 10/1000/year at age of 90. Elderly is susceptible to

post-herpetic neuralgia with over 50% suffered from this complication after 60 years of age. Systemic anti-viral therapy such as acyclovir is indicated if it can be given within 72 hours from onset, in disseminated herpes zoster or in immunocompromised patients.

### *Skin tumours*

Most skin tumours are more common in the elderly. Benign lesions like seborrhoeic keratosis or malignant lesions, particularly basal cell carcinoma and squamous cell carcinoma may occur.

Basal cell carcinoma (BCC) is the most common malignant skin tumour and is related to solar radiation. It is believed to arise from the hair follicles. It is locally invasive and rarely metastasises. Pigmented BCC is the commonest BCC type in Chinese. Treatment is mainly by surgical excision or Moh's micrographic surgery. Other modalities include radiotherapy and topical imiquimod.

Squamous cell carcinoma is a malignant neoplasm, less frequently seen than BCC but tends to metastasise. The lesions appear as erythematous, keratotic papules or nodules with or without ulceration. It may arise from pre-malignant lesions such as actinic keratosis or

Bowen's disease. Assessment includes examination for lymphadenopathy and organomegaly and imaging for metastasis. The main stay of therapy is surgical excision and radiotherapy.

### *Mycosis fungoides*

It is an indolent primary cutaneous T-cell lymphoma that affects mainly the elderly. It may mimic all kinds of inflammatory dermatoses and easily leads to misdiagnosis. It remains in patch stage for years before evolving to plaque or tumour stage. The plaques are well defined and scaly, dusky or violaceous in colour and may be indurated. Lesions in cutaneous stages may regress or coalesce to form larger plaques with bizarre configuration. Clinical staging looking for lymph node or visceral involvement is essential. Treatment depends on clinical staging and includes topical steroid, topical nitrogen mustard, phototherapy, total electron beam irradiation, local radiotherapy or interferon.

### ***Learning points:***

*When managing elderly patients with skin rash, important issues to consider after an accurate diagnosis include issues of compliance, feasibility of drug application and higher risks of adverse drug reactions and side effects.*