Social Hygiene Symposium 2003

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Abnormal Paps smear – gynaecological management

Speaker: Dr. T.C. Pun
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A protocol for the management of abnormal cervical smears in the local settings is available at the website of the Hong Kong College of Obstetricians and Gynaecologists. The decision for referral for colposcopic examination depends on the likelihood of developing cervical in-situ neoplasia (CIN)-II/III or more advanced stage. For atypical squamous cell of unknown significance (ASCUS), a repeated smear in four to six months is suggested and referral should be made if abnormality still persists. Other gradings such as atypical squamous cell-high grade, low or high-grade squamous intraepithelial lesion (LSIL/HSIL) and atypical glandular cells (AGC) should be referred for colposcopic examination. As grading such as HSIL cannot exclude invasion and invasive cancer, early referral should be made.

Colposcopy allows magnification of cervix for biopsy. If a gross lesion is seen, immediate biopsy should be performed instead of waiting for colposcopic examination. Satisfactory colposcopy requires adequate exposure of the transformation zone, which is the area most susceptible to human papillomavirus (HPV) infection. Acetowhite epithelium describes the transient appearance of white lesion in area of high nuclear density, which may indicate CIN or other possibilities such as HPV infection. Identification of abnormal cervical lesion can also be assisted by the application of iodine solution. Features suggestive of invasion on colposcopy are abnormal vessels, irregular surface and large complex lesion.

For CIN-I, 85% of cases will regress after two years; therefore regular follow up is suggested. Treatment is suggested if CIN-I involves more than two quadrants of the cervix or the patient is unable to follow up or the lesion persists for more than two years. For higher-grade lesions, treatment is warranted. The most common mode of treatment is large loop excision of the transformation zone, also called loop electrosurgical excision procedure. The most common side effect is bleeding either intra- or post-operatively, whereas infection, cervical stenosis and cervical deformity are rare complications.

For AGC-endocervical cells, colposcopy, biopsy and endocervical sampling are suggested. On the other hand, for AGC-endometrial cells, endometrial sampling is usually performed first and when it is normal, further investigation such as colposcopy and endocervical sampling will be needed. For endometrial cells in cervical smear after menopause, further investigation is recommended. If endometrial cells are found in cervical smear before age of 40, no further

investigation is needed. But for endometrial cells in cervical smear after age of 40, smear result should be correlated with clinical findings to determine the management.

Before taking cervical smear, it is important to provide adequate information to the patient in order to allay their anxiety. In United Kingdom, the most common reason to call back patient is unsatisfactory smear. The Hong Kong Society for Colposcopy and Cervical Pathology and the Hong Kong College of Obstetricians and Gynaecologists have established mechanisms for accreditation and reaccreditation of colposcopists and colposcopy service.

Learning points:

The urgency for referral of abnormal cervical smear depends on the type of abnormality. The Hong Kong College of Obstetricians and Gynaecologists has developed a protocol for the management of abnormal cervical smear.

Life Threatening Dermatoses

Speaker: Dr. S.Y. Cheng
Medical and Health Officer, Social Hygiene Service, Department of Health

Life threatening dermatoses can be classified aetiologically into infectious diseases, serious drug eruptions, primarily dermatological disorders, serious medical diseases with prominent cutaneous manifestations and skin tumours. For the above four etiological categories, clinical morphology ranges from generalised erythematous lesions, erythema with desquamation of skin, vesiculobullous lesions, pustular lesions to purpuric lesions.

For example, generalised erythematous lesions can occur in toxic shock syndrome. The syndrome is caused by toxin producing Staphylococcus aureus and is characterised clinically by fever, hypotension, generalised scarlatiniform eruption, multiorgan failure and desquamation of palm and soles one to two weeks later. In the past, the syndrome was linked to the use of highly absorbent vaginal tampon, but now cutaneous wound, nasal packing and postpartum infection are increasingly important as site of infection. The disease is toxin mediated and blood culture is only positive in five percent of cases. A similar syndrome can be caused by group A streptococcus. Erythroderma describes generalised redness and scaling of skin involving greater than 90% of body surface. It can be secondary to psoriasis, atopic dermatitis, drugs, cutaneous lymphoma, pityriasis rubra pilaris but the cause can be unknown in 20% of cases. Other manifestations of erythroderma include generalised lymphadenopathy, fever, malaise, ectropion, alopecia, keratoderma and nail dystrophy. Erythroderma is a medical emergency as it may be complicated by electrolyte and fluid imbalance, hypoalbuminemia, hypothermia, high output cardiac failure, adult respiratory distress syndrome and infection.

The second pattern is erythema with desquamation. Staphylococcal scalded skin syndrome is caused by epidermolytic toxins from Staphylococcus aureus. It presents with fever, cutaneous tenderness, erythema followed by generalised desquamation and the Nikolsky's sign is positive. When it occurs in children, mortality is about three percent. In adults, the mortality can be greater than 50% as it usually occurs in patients with chronic renal insufficiency or with immuno-suppression. Kawasaki's disease is characterised by high fever lasting more than five days, bilateral conjunctival injection, mucous membrane changes, diffuse scarlatiniform eruption, exfoliation over extremities and cervical lymphadenopathy. The disease usually affects children and can be associated with coronary artery aneurysm in 20% of cases. Toxic epidermal necrolysis (TEN) manifests by severe mucocutaneous erythema and exfoliation, often involving greater than 30% of body surface area. Most of the TEN are drug induced and sulphonamide, anticonvulsant, allopurinol and oxicam nonsteroidal anti-inflammatory drugs carry

a high risk of inducing TEN. Role of systemic corticosteroid in the management of TEN is controversial but there are successful reports of treatment by intravenous immunoglobulin.

Disseminated herpes and varicella infection and autoimmune blistering diseases are examples of life threatening vesiculobullous diseases. Risk factors for disseminated herpes and varicella infection are immunosuppressed state such as organ transplant recipients and haematologic malignancy. Internal organ involvement such as pneumonitis or hepatitis can be severe in immunocompromised patients. Pemphigus vulgaris and bullous pemphigoid are induced by autoantibodies to antigens of desmosomes and hemidesmosomes respectively. Clinically, bullous pemphigoid has less readily ruptured blisters and occurs in older age patients as compared with pemphigus vulgaris.

Pustular eruptions can either be sterile such as pustular psoriasis or non-sterile such as disseminated gonococcal infection. Pustular psoriasis can be precipitated by pregnancy, infection, drugs and tapering of steroid therapy. Non-pregnant patients can be managed with acitretin, methotrexate, phototherapy or cyclosporin. Disseminated gonococcal infection is characterised by fever, asymmetrical arthritis or tenosynovitis and few number of pustular or petechial skin lesions. Culture of skin lesions, synovial fluid and blood may yield positive results in 10-30% of cases. Systemic cephalosporin such as ceftriaxone is often employed for gonococcal infection.

Multiple infectious diseases can cause life threatening purpuric dermatosis. Meningococcemia is caused by Neisseria meningitides. It is characterised by fever, hypotension, meningitis and petechial lesions of skin or mucosa. In advanced stage, pneumonia, endocarditis, pericarditis, shock and disseminated intravascular coagulation can be present. In necrotising fasciitis, rapidly progressive necrosis of fat and subcutaneous tissue is caused by group A streptococcus and/or other bacteria. It presents clinically with erythematous hot and tender erythema/purpura over the extremities. In advanced stage, violaceous bullae, necrosis of fascia with malodorous discharge and shock can be seen. Surgical debridement together with parental antibiotics is essential in treatment of necrotising fasciitis.

Learning points:

Several dermatoses can be life threatening and may need in-hospital management. History and recognition of the clinical pattern can guide appropriate investigations to confirm diagnosis.

Update Treatment in Psoriasis

Speaker: Dr. K.H. Lau
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Psoriasis is a common skin disease and it is estimated that 2% of the population are affected. In Hong Kong, there were more than 1500 new psoriatic patients seen in the Social Hygiene Service in 2002, accounting for about 4% of all new skin cases. It was the fifth most common new skin consultation in the service.

The knowledge on pathogenesis of psoriasis has undergone changes in recent years. Previously considered as chronic inflammatory disease of unknown cause, the importance of T-lymphocytes in mediating the inflammatory changes has been increasingly recognised. Psoriasis is a Th-1 mediated inflammatory response. As such, the Th-1 cytokines (interleukin-2, interferon-γ and tumour necrosis factor (TNF)-α) are produced in the skin lesion, leading to recruitment of inflammatory cells from the circulation, keratinocyte proliferation and proliferation of new blood vessels. Besides the interaction of antigen/major histocompatability complex with CD4/8, the importance of additional co-stimulatory molecules interaction in activation of T-cells has also been

recognised and is employed in the new biologic treatment of psoriasis.

Topical treatment, phototherapy and systemic therapy are the three important therapeutic modalities in the management of psoriasis. They have different mechanism of action and side effect profile. They can be used alone, in combination, in rotation or in sequence to achieve therapeutic efficacy while minimising the side effects. The choice depends on the clinical disease, patient factors as well as physician's consideration.

For topical therapy, a new dithranol preparation in a temperature sensitive vehicle has been developed. It releases the active drug at skin temperature and hence causes less staining and irritation. Newer topical steroid with improved benefit to risk ratio (for example, fluticasone propionate, mometasone furoate and prednicarbate) are also used for psoriasis treatment. New topical vitamin D3 analogue, such as calcitriol has been recently introduced. It is less irritative than traditional vitamin D3 analogue and can be used in flexural area and hairline as well. Combination of topical vitamin D3 analogue with corticosteroid has also been developed, which causes less irritation and is faster acting than traditional vitamin D3 analogue alone. Topical vitamin A derivative, tazarotene, has also been used in psoriasis and it can be combined with phototherapy to achieve a synergistic effect.

For phototherapy, narrow band ultraviolet B (UVB), which emits radiation around the wavelength of 311 nm, is now a widely used treatment for psoriasis. Its efficacy is better than broadband UVB but is probably less carcinogenic than photochemotherapy. Excimer laser, emitting radiation at 308 nm, has also been used for refractory psoriatic plaques. It seems to offer rapid clearance and induces longer clinical remission. But because of size of hand piece, it is very time consuming if a large surface area of psoriasis is to be treated. Ongoing studies will find out the optimal regimen in applying this laser for psoriasis.

Methotrexate is very useful in refractory plaque psoriasis involving a large surface area. One of the major disadvantage of this drug is the need for liver biopsy every 1.5 g cumulative dose, which carries a small risk of procedure related morbidity and mortality. Recent work has been focused on the use of measuring the serum level of aminopeptide of type III procollagen to detect the early changes of liver cirrhosis. It is hoped that the test can reduce the necessity of liver biopsy. Acitretin is useful for pustular and erythrodermic psoriasis but is slower acting, whereas cyclosporin is faster acting and is useful for flare or recalcitrant psoriasis. A sequential therapy has been proposed in psoriasis flare. Cyclosporin is used early in disease flare to gain rapid control. Then substitution with acitretin is made in the maintenance phase. Theoretically, the fast action of cyclopsorin can thus be employed while reducing the long-term side effect profile of nephrotoxicity. Both drugs have different side effect profiles except for raised lipid level.

New biologic agents targeting co-stimulatory molecules interaction and cytokines are in early phase of marketing or final stages of clinical trials. Alefacept is a fusion protein of human lymphocyte function associated antigen (LFA)-3 and Fc portion of human IgG1 that binds to CD2 on T cells. Efalizumab is a humanised monoclonal antibody that binds to human LFA-1 and blocks both activation and migration of T-lymphocytes. Etanercept is a recombinant human TNF-α receptor fusion protein and infliximab is a monoclonal antibody directed against TNF-α. They are the new options in the management of psoriasis.

Learning points:

Advances in treatment of psoriasis have been made both in terms of development of new drugs/vehicle/drugs combination that has a better benefit to risk ratio and introduction of new biologic treatment targeting T-lymphocyte mediated inflammation.