

Journal Watch

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Extramammary Paget's disease: outcome of radiotherapy with curative intent

Luk NM, Yu KH, Yeung WK, Choi CL, Teo ML.
Clin Exp Dermatol 2003;28:360-3.

The role of radiotherapy as curative treatment of extramammary Paget's disease (EMPD) has not been well studied. The authors reported their experience of using radiotherapy in treating EMPD. Six patients (five male, one female) with EMPD diagnosed between 1984 and 2001 were included. Two patients had associated underlying adenocarcinoma. Two patients received radiotherapy as primary treatment, three as definitive treatment for relapse after excision and one as postoperative adjuvant therapy. Radiotherapy techniques included high dose rate mould brachytherapy, electron beam, superficial X-ray and photon treatments.

Five patients had complete response while one had partial response. The follow-up duration after radiotherapy was 1.2-14.8 years. One complete responder had a local relapse and was successfully salvaged by surgery. The two patients with underlying carcinoma died of distant metastasis at 14 and 15 months after radiotherapy. Confluent wet desquamation occurred in all patients during radiotherapy but only required treatment interruption.

The authors concluded that radiotherapy might play a role in the management of EMPD. However, more studies are required to determine the optimal radiation dose. In addition, the possibility of more aggressive local treatment such as

combined chemoradiotherapy and systemic chemotherapy may also be explored.

Cutaneous and pulmonary sarcoidosis in a Hong Kong Chinese woman with silicone breast prostheses

Chang KC, Chan KT, Chong LY, Lau KS, Tam CM, Lam CW.
Respirology 2003;8:379-82.

Sarcoidosis is considered rare in Chinese. This was a case report of cutaneous and pulmonary sarcoidosis in a 54-year-old Chinese woman. The patient presented with insidious onset of multiple erythematous lesions over the face and neck. Skin biopsy revealed granulomatous inflammation with negative stain for acid-fast bacilli. She had undergone silicone breast augmentation surgery four years earlier.

Anti-tuberculosis therapy was started for suspected lupus vulgaris and then was stopped two months later because of poor clinical response. Subsequently a right supraclavicular lymph node was found and aspirated, showing granulomatous inflammation. The subsequent chest X-ray showed diffuse reticulonodular opacities and mild right pleural effusion. High-resolution CT of the thorax showed features consistent with sarcoidosis, including mediastinal lymphadenopathy and diffuse perilymphatic nodular opacities. Sputum mycobacterial culture was negative while the fiberoptic bronchoscopy showed no endobronchial lesion. However, the transbronchial

biopsy also showed granulomatous inflammation with no evidence of infection, malignancy or foreign body. Pulmonary function tests were normal except for an impaired transfer factor. The serum angiotensin-converting enzyme levels were elevated. The patient was managed conservatively. One year later, majority of the cutaneous lesions resolved spontaneously. The chest X-ray showed minimal change in the lung field and the right pleural calcification partially improved. The authors also postulated that the silicone elastomer material contained in the breast prostheses might be the aetiological factor in this particular patient. The removal of breast implants should be considered if the patient's clinical condition deteriorates.

Oral retinoid use reduces cutaneous squamous cell carcinoma risk in patients with psoriasis treated with psoralen-UVA: a nested cohort study

Nijsten TEC, Stern RS.

J Am Acad Dermatol 2003;49:644-50.

The risk of developing squamous cell carcinoma is increased among psoriatic patients who had received psoralen-UVA (PUVA). Small open studies suggested that oral retinoids might be useful to reduce skin cancer risk in patients at high risk. This nested cohort study was performed to assess whether systemic retinoid reduced skin cancer risk among psoriatic patients who had been exposed to PUVA.

From 1985 to 2000, 135 of the 1380 patients in the PUVA Follow-up Study used systemic retinoid for at least 26 weeks in one year or more. For each patient, the incidences of squamous cell carcinoma and basal cell carcinoma during the years of substantial systemic retinoid use were compared with those in the other years. Poisson regression model was used to adjust for cofounders. In paired analysis, oral retinoid use at doses of 25 mg/day or more was associated

with a 30% reduction in the incidence of squamous cell carcinoma (196/1000 years of use vs 302/1000 years of no use; $p=0.002$). After adjusting for other associated risk factors, the incidence of squamous cell carcinoma was significantly reduced during the years of substantial systemic retinoid use (incidence rate ratio=0.79; 95% confidence interval=0.65, 0.95). However, systemic retinoid use did not alter the incidence of basal cell carcinoma.

The authors concluded that systemic retinoid use reduced the risk of developing squamous cell carcinoma in psoriatic patients treated with PUVA. However, the long-term side effect of systemic retinoid must be balanced against their potential beneficial anticancer effects.

Specific site involvement in fixed drug eruption

Özkaya-Bayazit E.

J Am Acad Dermatol 2003;49:1003-7.

The aim of this study was to investigate the drug-related site involvement of fixed drug eruption. A total of 105 patients (52 female; 53 male) with the diagnosis of fixed drug eruption confirmed after oral provocation test were evaluated. The data concerning the sites of eruption and the inducer drugs were subjected to hierarchical cluster analysis to identify clusters of drug eruption sites related to certain drugs.

At the time of diagnosis, 15 patients (14.3%) had had their first attack whereas 16 (15.2%) had had more than 10 attacks. Cotrimoxazole was the most common causative agent (63.8%), followed by naproxen sodium (23.8%), dipyrone (5.7%), oxicams (4.8%) and others (1.9%). Cotrimoxazole most frequently induced lesions on genital mucosa; naproxen and oxicams on lips; and dipyrone on trunk and extremities. Significant association could be established between naproxen and fixed drug eruption on lips (chi-

square=28.3; $p<0.001$). On the other hand, isolated involvement of male genitalia was exclusively due to cotrimoxazole.

The author concluded that naproxen should be considered as an important potential cause of fixed drug eruption on lips. Similar large studies and regularly updated lists concerning the specific site involvement associated with specific drugs would be most useful to clinicians evaluating patients with suspected fixed drug eruption.

Topical bexarotene therapy for patients with refractory or persistent early-stage cutaneous T-cell lymphoma: results of the phase III clinical trial

Heald P, Mehlmauer M, Martin AG, Crowley CA, Yocum RC, Reich SD, for the members of the Worldwide Bexarotene Study Group.
J Am Acad Dermatol 2003;49:801-15.

Bexarotene is a synthetic retinoid that activates the retinoid X receptor. This multinational, open-label, phase III study aimed at determining the safety and efficacy of topical 1% bexarotene gel in 50 patients with refractory or persistent stage IA to IIA cutaneous T-cell lymphoma. Bexarotene was applied topically to all lesions for at least 16 weeks. The frequency of application was escalated at one-week intervals from every other day to once, twice, thrice and then four times daily, as tolerated. The primary end point classification was the overall complete and partial response rate by the higher of the two measures: Physician's Global Assessment of Clinical Condition (score 0 to 6 according to clinical improvement) and the Composite Assessment of Index Lesion Disease Severity (grading according to clinical signs including erythema, scaling, plaque elevation, hypo/hyper-pigmentation and surface area).

The overall response rates for the Physician's Global Assessment of Clinical Condition, the

Composite Assessment of Index Lesion Disease Severity, and primary end point classification were respectively 44%, 46% and 54%. The median time to response was 142 days. The most common adverse events were mild to moderate dose-related irritant dermatitis, pruritus and local burning pain. No major adverse events were reported.

The authors concluded that topical bexarotene was a well-tolerated and effective treatment in patients with refractory or persistent early-stage cutaneous T-cell lymphoma. However, there may be practical limitations of application of gel over a large area and the tolerability of irritant dermatitis in individual patients.

Low-dose methotrexate to treat mycosis fungoides: a retrospective study in 69 patients

Zackheim HS, Kashani-Sabet M, McMillan A.
J Am Acad Dermatol 2003;49:873-8.

Low-dose methotrexate has been used to treat mycosis fungoides. This retrospective study summarised the authors' experience in using low-dose methotrexate to treat 69 patients with patch/plaque and tumour stage mycosis fungoides and who had failed previous treatment, since February 1981.

Sixty patients belonged to the stage T2 disease (>10% skin involved) while only two patients were in T1 disease (<10% skin involved). The remaining seven patients were in T3 disease (tumour stage). The follow up periods ranged from one to 201 months with a median of 15 months. Of patients in stage T2, seven (12%) achieved complete remission and 13 (22%) achieved partial remission making a total response rate of 33% (20/60). Only one out of seven patients in tumour stage responded. The maximum dose was usually 50 mg once weekly and the median weekly dose was 25 mg. The median time to treatment failure

was 15 months. The side effects included oral mucositis or stomatitis (17.4%), gastrointestinal disturbances (15.9%), bone marrow depression (13%), neurologic symptoms (8.7%) and elevated transaminase levels (6%).

The authors concluded that low-dose methotrexate might be of value to treat a subset of patients with plaque/patch mycosis fungoides resistant to other therapies. The major drawback of this study was the small sample size and the short follow up time. In addition, the role of methotrexate in transformation of mycosis fungoides needs to be further evaluated in future study.

Sentinel lymphonodectomy in nonmelanoma skin malignancies

Michl C, Starz H, Bachter D, Balda BR.

Br J Dermatol 2003;149:763-9.

This study investigated the use of sentinel lymphonodectomy in 37 patients (18 males, 19 females) with various cutaneous high-risk stage N0 non-melanoma skin cancers. There were 11 patients with squamous cell carcinomas, seven with Merkel cell carcinomas, five with cutaneous lymphomas, eight with adnexal carcinomas and six other skin cancers. Basal cell carcinoma was not included because they usually did not metastasise. None had evidence of lymph node involvement or systemic tumour dissemination at the time of presentation.

All 37 patients underwent sentinel lymphonodectomy after lymphoscintigraphy. The procedure was performed by the same team and there was no complication related to the procedure. After sentinel lymphonodectomy 28 patients showed no lymph node involvement and the remaining nine patients showed micrometastases in the sentinel lymph nodes with five of them underwent radical lymph node dissection within two weeks from sentinel

lymphonodectomy. During a mean follow-up period of 2.5 years (2 months-4.5 years), there was no evidence of tumour dissemination in 23 patients with negative sentinel lymph nodes. Four other patients with negative sentinel lymph nodes died of unrelated causes and one had extra-nodal metastasis in the parotid gland. Sentinel lymphonodectomy therefore seemed to be a sensitive tool in detecting early lymphonodular microinvolvement in patients with high-risk stage N0 non-melanoma skin cancers. Extensive surgical interventions can be avoided in patients with negative sentinel lymph nodes. Nevertheless, follow up studies are needed to evaluate the long-term benefit of sentinel lymphonodectomy in nonmelanoma skin malignancies.

Guidelines for the management of alopecia areata

MacDonald Hull SP, Wood ML, Hutchison PE, Sladden M, Messenger AG.

Br J Dermatol 2003;149:692-9.

Alopecia areata is an autoimmune disease leading to patchy or diffuse hair loss on the scalp and may affect any part of the hair-bearing skin. A number of treatments can induce hair growth in alopecia areata but none can alter the course. The followings are evidence-based guidelines for the treatment of alopecia areata, prepared on behalf of the British Association of Dermatologists.

Patients with short duration of limited patchy hair loss can be managed by reassurance alone, as spontaneous remission occurs in up to 80% of these cases. There is little evidence to support the use of potent topical corticosteroids for alopecia areata and it is ineffective in alopecia totalis and alopecia universalis. There is fair evidence to support the use of intralesional depot corticosteroid in limited alopecia areata. It is however not effective in rapidly progressive alopecia nor in extensive disease. Although continued or pulsed systemic corticosteroids and

PUVA can produce regrowth of hair in some patients, they are not recommended owing to their potentially serious side effects and inadequate evidence of efficacy.

A review of all published data of contact immunotherapy with squaric acid dibutylester or 2,3-diphenylcyclopropenone showed that 50-60% (range: 9-87%) of patients achieve a worthwhile response. Contact immunotherapy is thus recommended for extensive patchy loss and is the only treatment likely to be effective in alopecia totalis and alopecia universalis, although the response rate is still low. Furthermore, there is no convincing evidence for the use of dithranol and minoxidil lotion in treating alopecia areata.

Comparison of trichloroacetic acid solution and cryosurgery in the treatment of solar lentigines

Lugo-Janer A, Lugo-Somolinos A, Sanchez JL.
Int J Dermatol 2003;42:829-31.

Cryotherapy with liquid nitrogen and 30% trichloroacetic acid has been shown to be effective in the treatment of solar lentigines. They are relatively cheap and cost-effective. Twenty-five female patients with marked evidence of solar lentigines over the dorsa of each hand were randomised to receive a one-time treatment of either 30% trichloroacetic acid to be applied till an even frosting occurred; or cryotherapy delivered with a 0.3-mm tip at 3 cm from the lesion for one to five seconds after initial freezing. Digital photographs were taken under the same settings before and eight weeks after treatment for evaluation of treatment efficacy by three blinded observers. They graded the degree of lightening according to a 4-point scale: no improvement, <20%; mild improvement, 20-50%; moderate improvement, 51-75%; marked improvement, >75%. Nine patients (47%) in the trichloroacetic acid group achieved more than 50% improvement compared with 15 patients

(71%) in the cryosurgery group ($P<0.05$). It was noted that 86% of the patients with skin type II achieved more than 50% improvement compared with 50% and 33% of the patients with skin types III and IV. Cryotherapy was more painful and took longer to heal. There was no complication (such as atrophy or hypopigmentation) seen in all cases except one case of hypertrophic scar. Thus, these two old-fashioned treatments are both cost-effective and safe. The drawback of this study is that cryotherapy was not delivered by a single person and inter-operator variations might affect the outcome of the treatment.

Calcipotriol versus coal tar: a prospective randomised study in stable plaque psoriasis

Sharma V, Kaur I, Kumar B.
Int J Dermatol 2003;42:834-8.

Thirty-six patients with nearly symmetrical stable plaque psoriasis were recruited to a 12-week prospective, right-left randomised, investigator-blinded study to compare the effectiveness of 0.005% calcipotriol ointment and 5% coal tar ointment. All other medications were stopped four weeks before the study and only coconut oil as emollient was allowed during the study period.

Calcipotriol was applied twice daily and coal tar overnight on each side of the body. The patients were advised to receive two hours of sun exposure every day. All patients were assessed by the same physician using the ESI (erythema, scaling, induration) score. Serum biochemical parameters, like calcium, phosphate, alkaline phosphatase, 24-h urinary calcium and phosphate were assayed. Thirty patients (21 males and 9 females) completed the study. The mean baseline ESI score was 29.5 ± 4.3 . The median time for attaining significant improvement (>50% reduction in the ESI score) with calcipotriol was significantly shorter than that with coal tar, namely 6.1 ± 1.9 weeks vs. 9.6 ± 1.8 weeks ($p<0.001$). However, at 10

and 12 weeks, the differences in ESI score were insignificant between the two groups. The biochemical parameters remained unchanged throughout the study period. Relapse, defined as an increase of 25% in the last ESI score, was found in 10% of patients treated with calcipotriol compared to 16.7% of patients treated with coal tar ($P>0.05$) during a follow-up period of eight weeks.

Hence, the initial response with calcipotriol ointment was faster but the long-term efficacy appeared similar. There was also no statistically significant difference in the relapse rates. Calcipotriol is more cosmetically acceptable but the enormous cost difference is also an important consideration.

Clinical study of 40 cases of incontinentia pigmenti

Hadj-Rabia S, Froidevaux D, Bodak N, Hamel-Teillac D, Smahi A, Touil Y, et al.
Arch Dermatol 2003;139:1163-70.

The objective of this study was to analyse the distribution of clinical features in incontinentia pigmenti (IP) and define guidelines for follow-up. The clinical records of 40 paediatric patients (3 boys, 37 girls) diagnosed with IP were reviewed. In particular, cutaneous, neurological, ocular and dental manifestations were evaluated. The median age at diagnosis was 6 months 9 days (range: birth to 12 years). Cutaneous signs were present as early as one day after birth and appeared in the following order: 37 cases (92%) with stage 1; 32 cases (80%) with stage 2; 36 cases (90%) with stage 3; and 12 cases (30%) with stage 4. These stages were not present in all patients.

Thirteen patients (32%) had neurological abnormalities such as seizures (10 cases, 77%), delayed psychomotor development (7 cases, 54%), and mental retardation (3 cases, 23%). Neuroimaging showed abnormalities such as

cerebral atrophy, haemorrhagic necrosis, porencephalia in 10 out of 12 cases. Ocular abnormalities including strabismus, unilateral microphthalmia and retinal detachment were found in 7 out of 34 cases (20%). Dental abnormalities were present in 10 out of 17 cases (59%). There was a positive family history in 11 of 40 cases (28%). The three male cases were considered to be sporadic forms.

The authors concluded that the diagnosis of IP was still based on clinical criteria although molecular techniques might be helpful in borderline cases. Multidisciplinary follow-up is required, especially in the first year of life to detect neurological or ocular abnormalities.

Nodular amyloidosis: review and long-term follow-up of 16 cases

Moon AO, Calamia KT, Walsh JS.
Arch Dermatol 2003;139:1157-9.

This is a retrospective study analysing the clinical presentation of 16 patients with biopsy-proven nodular amyloidosis. There were nine women and seven men. The mean age at diagnosis was 60.8 years (range 41-87 years) and the mean duration of lesion before diagnosis was 13.5 years. Immunohistochemical analysis was performed to detect κ and λ light chain restriction. Patients were also assessed by telephone for progression to systemic amyloidosis.

Acral lesions were most common (eight patients), although lesions were also found on the nose, feet, and periauricular areas. Associated diseases were Sjögren's syndrome (two patients), type two diabetes mellitus (two patients), and liver disease (three patients). Kappa and λ light chain restriction was detected in four patients and two patients respectively, suggesting plasma cell clonal proliferation. One patient developed systemic amyloidosis. She was noted to have a serum monoclonal IgG λ protein at diagnosis and died

four years later. Her lung biopsy confirmed interstitial amyloidosis. Follow-up data for 14 of the remaining patients showed no evidence of systemic amyloidosis (follow-up period 10 years, range 8 months to 24 years).

The authors concluded that the acral areas were common sites for nodular amyloidosis and that progression to systemic amyloidosis was uncommon. The frequent finding of light chain restriction in these cases suggests the presence of a local plasma cell clone.

Mucocutaneous findings in paediatric AIDS related to degree of immunosuppression

Wananukul S, Deekajorndech T, Panchareon C, Thisyakorn U.

Pediatr Dermatol 2003;20(4):289-94.

This study investigated the prevalence of mucocutaneous disease in 120 paediatric AIDS patients (59 boys, 61 girls) less than 13 years of age. Patients were classified according to the degree of immunosuppression based on the percentage of CD4-positive lymphocytes as follows: no evidence of immunosuppression ($\geq 25\%$), moderate immunosuppression (15-24%), and severe immunosuppression (1-14%).

Mucocutaneous disease was significantly more common with increasing immunosuppression (62%, 43% and 20% in those with severe, moderate and no immunosuppression, respectively). The prevalence of two mucocutaneous diseases in moderate immunosuppression group was 11%. In patients with severe immunosuppression, 21% had two or more mucocutaneous findings. Infection was the most common finding (55%). Fungal infection was found in 44% of patients, of which oral candidiasis was most common (33%). Viral infections and bacterial infections were found in 10% and 8% patients respectively. Viral infections including herpes zoster (6%), chronic

herpes simplex (5%), and molluscum contagiosum (2%), affected patients with moderate to severe immunosuppression. Herpes zoster and chronic ulcerative herpes simplex stomatitis were found in patients with a mean percentage of CD4-positive lymphocytes of 13.5%, and 3% respectively. Bacterial infections included impetigo and abscesses caused by *Staphylococcus aureus* and acid-fast bacilli. Non-infectious conditions included papular pruritic eruption (6.3%), drug reaction, seborrhoeic dermatitis and ichthyosis; all of which were more common in those with severe immunosuppression.

The authors concluded that mucocutaneous manifestations were common in paediatric AIDS patients and many were infectious in origin. Patients with severe immunosuppression may present with more than one mucocutaneous manifestation. As this is a cross-sectional study, follow-up studies on the course of mucocutaneous disease in paediatric AIDS patients are needed.

Genital carriage of human papillomavirus (HPV) DNA in prepubertal girls with and without vulval disease

Powell J, Strauss S, Gray J, Wojnarowska F.

Pediatr Dermatol 2003;20 (3):191-4.

There has been evidence to suggest a link between lichen sclerosus (LS) and human papillomavirus (HPV). This study aimed to determine the rate of HPV carriage in girls with LS compared to those with non-LS vulval disease and those without vulval disease.

Vulval scrapes and urine samples were collected from girls with LS and non-LS vulval disease and were analysed for HPV DNA by nested PCR. Thirty-two girls with LS, 31 girls with non-LS vulval disease and 29 girls with no vulval disease (controls) were studied (age range 2-11 years). HPV DNA was found in the urine and vulval scrapes

of eight girls (25%) with LS, two girls (6.5%) with non-LS vulval disease and in the urine of seven girls (24.1%) in the control group. The frequency of HPV in LS was not significantly increased. Girls with LS were associated with HPV types of high (HPV 16, 18) or intermediate-risk (HPV 31, 34 and 53) for dysplasia. In the controls and girls with non-LS vulval disease, low (HPV 6 and 11) or intermediate risk types were more common. Mothers of 15 girls (46.9%) with LS had had an abnormal cervical smear within three years of

delivery and mothers of two girls with LS had anogenital warts.

It was concluded that LS patients carried high-risk and intermediate-risk HPV types for dysplasia and their mothers had had a high incidence of dyskaryotic smears. In addition, these findings suggest that HPV carriage in prepubertal girls seems to be common. It was suggested that studies with larger samples and longer follow-up were needed to determine the course of HPV carriage.