ORIGINAL ARTICLE

Paraneoplastic Dermatomyositis: A 12-year Retrospective Review in the Department of Dermatology Hospital Kuala Lumpur

M M Tang, M D(UKM), MRCP(UK), AdMDerm; S Thevarajah, MMed

Department of Dermatology, Hospital Kuala Lumpur, Jalan Pahang, 50586 Kuala Lumpur

SUMMARY

Adult-onset dermatomyositis has been found to be associated with underlying malignancies in up to 40% of patients. The aims of this study were to determine the demographic profile, the underlying cancer and outcome in patients with dermatomyositis. This was a retrospective review of 38 patients with dermatomyositis seen over a 12-year period in the Department of Dermatology, Kuala Lumpur Hospital. Of these, 18 (47.4%) had an associated underlying malignancy. The male to female ratio was 2:1. Ten patients (55.6%) were Chinese. The youngest patient encountered was 32 years old. Nasopharyngeal carcinoma (61.1%) was the most common malignancy in our study population. Tumour markers were not useful as the initial screening for malignancies. Thorough screening for malignancy is imperative in adult dermatomyositis especially those above 40 years old.

KEY WORDS:
dermatomyositis, paraneoplastic, nasopharyngeal carcinoma

INTRODUCTION

Dermatomyositis has been defined as an idiopathic myositis with distinctive cutaneous manifestations[1]. It however encompasses heterogenous subgroups of patients such as those with a strong association with malignancy; those with features of other connective tissue diseases and have a high level of autoantibodies such as anti Mi-2, anti-ku and anti-RNP; those with the existence of a separate cutaneous form without muscle damage i.e the amyopathic dermatomyositis; those with the absence of autoantibodies or malignancies i.e. the true idiopathic type; and those which are drug induced[3].

Paraneoplastic dermatomyositis has been reported to be as high as 40% in some cohort. A large population based study quoted a rate of about 20-25%[1]. Various types of malignancies have been described in paraneoplastic dermatomyositis. If we could identify the association of a specific type of cancers in this condition, it would help us greatly in early diagnosis of the malignancy.

The main objective in our review was to investigate the demographic data together with the clinical presentations of patients presented to us with dermatomyosistis and also to determine the association of any malignancy among them.

MATERIALS AND METHODS

The Department of Dermatology, Kuala Lumpur Hospital is a tertiary dermatology referral centre in Malaysia. In this 12-year retrospective review, the case records of patients who presented with dermatomyositis to the Department of Dermatology Hospital Kuala Lumpur from 16 August 1997 until 15 August 2009 were retrieved from the department computer system. The clinical features, diagnostic criteria, investigations for underlying malignancies and the outcome of patients were reviewed.

The diagnosis of dermatomyositis was based on the five Bohan & Peter criteria which include the presence of typical dermatologic features, symmetrical proximal myopathy, raised muscle enzymes, abnormal electromyogram and inflammatory myositis in muscle biopsy. The diagnosis of dermatomyositis is *definite* if there are presence of typical dermatologic features together with 3 or 4 other criteria. Otherwise the diagnosis would just be *probable dermatomyositis* if typical dermatologic features with 2 other criteria fulfilled; and *possible dermatomyositis* if typical dermatologic features with another criteria fulfilled.

The diagnostic workup to detect malignancies in adult patients with dermatomyositis was mainly guided by patients' symptoms. Some patients were already known to have a malignancy at the time of diagnosis of dermatomysitis. If patients were asymptomatic, we carried out a chest radiograph, complete blood count and tumor markers including alpha-Fetoprotein (□FP), Ca125 (for female patients), prostatic specific antigen (for male patients), carcinoembryonic antigen (CEA), and Ca19-9. As we are very concern about the fact that nasopharyngeal carcinoma (NPC) is the commonest malignancy associated with dermatomyositis in the Asian region, we carried out ear, nose and throat (ENT) assessment which included general examination of the ear nose and throat followed by biopsy of the fossa of Rosenmuller and CT scan of the paranasal sinuses. When NPC was excluded, upper and lower gastrointestinal scope, mammogram and pelvic examination in female patients, were performed.

RESULTS

For the past 12 years, we have seen 38 patients with dermatomyositis. The male to female ratio was 1.2:1. The mean age of presentation was 45.7 years old (15-74 years). The ethnic distribution was 44.7% for Malays, 44.7% for

This article was accepted: 29 June 2010
Corresponding Author: Min Moon Tang, Hospital Kuala Lumpur, Dermatology, Department of Dermatology, Hospital Kuala Lumpur, Jalan Pahang, 50586 Kuala Lumpur, Wilayah Persekutuan 50586, Malaysia Email: minmoon2005@yahoo.com

Chinese, 7.9% Indian and 2.6% others. All our patients (100%) presented with a photodistributed rash. Gottron's papules, which is a pathognomonic sign of dermatomyositis was presence in only 20 (52.6%) patients. Half of our patients (19) had poikiloderma and 44.7% of our patients had periungual telangiectasia. Although heliotrope rash is also a highly characteristic feature described in dermatomyositis, it appeared to be less commonly seen as only about a third of our patients (14 patients, 36.8%) had it. All our patients had proximal muscle weakness and they had raised muscle enzymes. Electromyogram was performed in 32 patients and of these 30 patients (93.7%) showed myopathic changes. Twenty seven patients underwent muscle biopsy and of these, 17 patients (62.9%) demonstrated inflammatory process in the muscle biopsy sample.

Out of 38 patients, 18 patients (47.4%) were those associated with underlying malignancies. The rest had idiopathic dermatomyositis (11 patients, 28.9%), dermatomyositis as part of their connective tissue disease (6 patients, 15.8%), and three patients (7.9%) who presented between the age of 15-17 years old were diagnosed to have juvenile dermatomyositis.

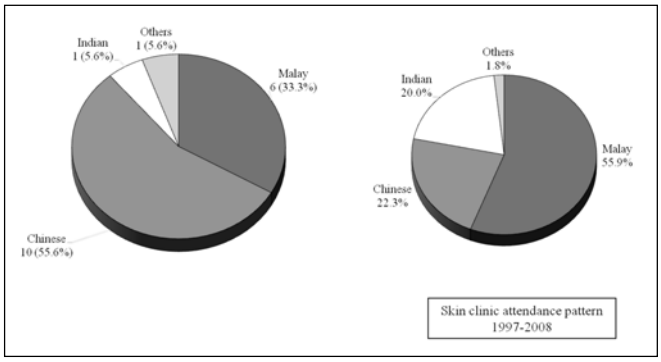

Fig. 1: Ethnic distribution of Paraneoplastic Dermatomyositis

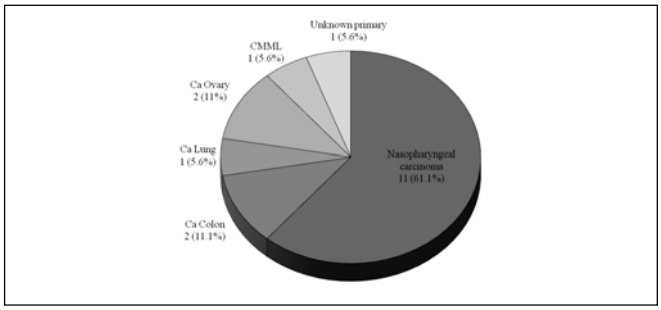

Fig. 2: Types of malignancies seen in paraneoplastic dermatomyositis

The mean age of patients with paraneoplastic dermatomyositis was 53.8 years old (range 32 - 73 years). Among the patients with dermatomyositis associated with malignancies, there was a male to female ratio of 2:1; as compared to the dermatology clinic attendance which the ratio was about equal. There were a larger proportion of Chinese patients making up to 55.6% of all patients affected as compared to the clinic attendance in which Chinese was about 22% (Figure 1). Looking at the types of malignancy, nasopharyngeal carcinoma (NPC) was the commonest malignancy (11 cases) contributing up to 61.1% of total cases (Figure 2). Interestingly, nine out of 11 NPC were Chinese; in fact 9 of the 10 Chinese patients in the cohort had NPC.

In term of the diagnosis of malignancies in relation to the onset of dermatomyositis, 7 patients had their malignancies diagnosed before the onset of dermatomyositis. Nine patients had their cancers diagnosed concurrently and 2 had their cancer diagnosed 3-6 months after the onset of dermatomyositis. In these 11 patients, we did chest radiographs for all patients and one turn out to be abnormal in which subsequent CT scan of the thorax and lung biopsy confirmed a small cell carcinoma of the lung. Tumor including FP, Ca125, Prostatic Specific Antigen, CEA, and Ca19-9 were all normal. All 11 patients had ENT assessment by ENT specialists and only 1 case showed an obvious mass. Three out of the 11 patients showed abnormal findings in the computed tomography (CT) scan of the paranasal sinuses. Biopsies of the fossa of Rosenmuller were carried out in 11 patients and out of these 7 were confirmed to be NPC. The remaining 4 patients with normal ENT examination had upper and lower gastrointestinal scope and 2 were diagnosed to have carcinoma of the colon. Two female patients had mammogram and pelvic examinations done and were found normal.

Table I is the summary of all 18 patients with paraneoplastic dermatomyositis. While waiting for the work up for malignancies patients were given prednisolone in the range of 30-75mg/day to treat muscle weakness. We were only able to taper down the dosage of prednisone after the primary malignancies were treated. In some patients, azathioprine, methotrexate and cyclophosphamide were used as adjuvant therapies. All the patients with nasopharyngeal carcinoma had radiotherapy. Patients who had carcinoma of the ovary, chronic myelomonocytic leukemia (CMML) and small cell carcinoma of the lung received chemotherapy. Seven patients died due to the underlying malignancies. Six defaulted follow up and the rest still under treatment.

DISCUSSION

Gottron's papules and heliotrope rash have been conventionally described as the pathognomonic and highly characteristic features respectively in dermatomyositis[1,2]. There were however not found in all of our patients. Rash in a photodistributed area was consistently present in all our 38 patients. Hence, in the absence of gottron's papules and heliotrope rash, a diagnosis of dermatomyositis should not be excluded if one presented with photodermatitis.

In various studies throughout the world, paraneoplastic dermatomyositis was reported at the rate between 15-43% (Table II & III). However the present series described a much higher percentage which was 47.4%. This figure nevertheless merely revealed the findings from one dermatology center which may not reflect the actual statistic of Malaysia. Besides dermatologists, Rheumatologists and General Internal Medicine Physicians are also managing cases with dermatomyositis in this region. Thus further audits from all the dermatology, rheumatology and general physician clinics including both public and private practice in this country should be encouraged to discover the true figure.

Hill *et al* reviewed the records of Scandinavian dermatomyositis and polymyositis and found 198 cases of 618 patients with dermatomyositis had cancer over a period of 20 years[13] (Table II). The study discovered that dermatomyositis was more strongly associated with ovarian,

Table I: Characteristics of 18 patients with paraneoplastic dermatomyositis

No	Age/race/sex	Diagnosis of DM	Cancer	Highest Pred dose required (mg/d)	Adjuvant therapy	Cancer Manage-ment	Outcome (from the diagnosis of malignancy)	Current/last Pred dose required (mg/d)
1	52 / C / M	Definite	NPC	75	Aza 100mg od	RT	Defaulted	60
2	64 / C / M	Definite	NPC	60	-	RT	Defaulted	10
3	65 / C / F	Definite	NPC	30	MTX 10mg/wk	RT	Died 4 yrs after diagnosis	20
4	51 / C / M	Definite	NPC	60	Aza 50mg od	RT	Alive, well 20mo	5
5	42 / C / M	Definite	NPC	50	Cycloph 50mg od	RT	Died 6mo after diagnosis	20
6	40 / C / F	Definite	NPC	45	-	RT	Defaulted	10
7	32 / C / M	Definite	NPC	60	-	RT	Alive well 14mo	10
8	62 / M / M	Probable	NPC	75	Aza 50mg od	RT	Alive well 18mo	35
9	44 / C / F	Probable	NPC	45	-	RT	Defaulted	10
10	52 / C / M	Probable	NPC	45	-	RT	Defaulted	10
11	59 / O / M	Definite	NPC	45	-	RT	Alive receiving RT	45
12	49 / I / F	Definite	Ca Ovary	60	-	Chemo	Died 7mo after diagnosis	30
13	66 / C / F	Definite	Ca Ovary	40	-	Chemo	Alive, well 12 mo	30
14	55 / M / M	Definite	Ca colon	75	-	Surgery	Defaulted	20
15	50 / M / M	Definite	Ca colon	40	-	Palliative	Died 5mo after diagnosis	10
16	73 / M / M	Definite	Lung Ca	75	-	Chemo	Died 6mo after diagnosis	50
17	49 / M / M	Definite	Occult	Declined	-	Palliative	Died 2mo after diagnosis	-
18	63 / M / F	Probable	CMML	40	-	Chemo	Died 11mo after diagnosis	10

M – Malay; C – Chinese; I – Indian; NPC – Nasopharyngeal carcinoma; Ca – Carcinoma; CMML – Chronic Myelomonocytic Leukaemia; Pred – Prednisolone; MTX – Methotrexate; Aza – Azathioprine; Cycloph – Cyclophosphamide; RT – Radiotherapy, Chemo – Chemotherapy; mo - months

lung, pancreatic, gastric, colorectal cancers and non-Hodgkin's lymphoma. In Tunisia, the cancers associated with paraneoplastic dermatomyositis were mainly breast (35%) and nasopharynx (25%)[12]. In Guangzhou China, Singapore and Taiwan where the main population is Han Chinese, nasopharyngeal carcinoma was the commonest associated malignancy giving a rate between 22-51.3%[3,10,16-17]. In the small series of Japanese literature however, the 2 most common cancers linked were uterine and lung carcinoma[15]. Nasopharngeal carcinoma in our current series outnumbered other malignancies in the association with dermatomyositis and 82% of them were Chinese patients. Further scrutiny revealed that the commonest type of cancers associated with DM of each country were actually among the 10 most common cancers in their individual cancer registry. Nonetheless the peculiar relation between NPC and adult Chinese patients with dermatomyositis warrants special attention including a detailed ENT assessment and blind biopsy of the fossa of Russenmuller Nasopharyngeal carcinoma is found to be endemic in south-eastern Asia and is related to the chronic active infection of Epstein–Barr virus (EBV)[18]. However, the titer of EBV antibodies was not assessed in our patients. Cases of chronic active EBV infection-induced generalized myositis have been reported by Hashimoto Y *et al*[19]. Furthermore, EBV was significantly detected in lung specimens from patients with rapidly progressive interstitial pneumonitis in polymyositis or dermatomyositis (PM /DM). Therefore, Huang YL *et al* proposed that the immune response to EBV in patients with NPC might possibly contribute to occurrence of DM/PM[17].

The risk factors of malignancy in the series of patients with dermatomyositis and/or polymyositis had been studied by many clinicians from various countries (Table III). Huang YL *et al* recently reported an increased risk of haematopoietic or lymphoid malignancy in Taiwanese children who has dermatomyositis[17]. There were also other case reports of malignancy occurred in young adults and even children with dermatomyositis, suggesting that age alone should not dissuade clinicians from careful assessment[3]. In this scenario the type of malignancy may be predicted according to the commonest cancer occurred the patients' age group.

The reports of the association between gender and the risk of malignancy in dermatomyositis were inconsistent. Mebazaa A *et al*[12] and Sigurgeirsson *et al*[6] reported that malignancy was more common in women. Nevertheless, Chen *et al*[10] and Wakata N *et al*[15] found that it was more common in men. In our series, there was a male predominance with a ratio of 2:1. Gender may not be the essential risk factor to predict paraneoplastic dermatomyositis but it may guide us on search of the underlying malignancies as certain cancers are more prevalence according to gender. A report from Taiwan has shown that among male patients with dermatomyositis, the most commonly associated cancer types were nasopharyngeal carcinoma followed by lung and liver cancer; whereas among female patients with dermatomyositis, the commonest cancer associated were the breast followed by lung and nasopharyngeal carcinoma[17].

Apart from the age of presentation, many clinicians have

been exploring other reliable methods that would predict the cancer risk in patients with dermatomyositis. Amoura Z *et al*[33] discovered that the risk of developing cancers is high in inflammatory myopathy patients during the first year following increased CA125 and/or CA19-9 levels. Thus the authors suggested that CA125 and CA19-9 assessment to be included in the search for cancer in dermatomyositis/ polymyositis patients, especially for inflammatory myopathy patients without interstitial lung disease. Nevertheless, tumour markers were not helpful in the initial screening for cancer in our current series likely because a considerable proportion of our patients have nasopharyngeal carcinoma for which a tumour marker is not available at present.

Kaji K *et al* from Japan found out that anti-155/140 antibodies are associated with cancer-associated dermatomyositis[20]. Chinoy *et al.* studied a large cohort of white adult patients with idiopathic inflammatory myopathy including dermatomyositis in the United Kingdom to predict the risk of associated cancer using myositis-specific antibodies[21]. Anti-155/140 was found to be dermatomyositis-specific with 50% sensitivity and 96% specificity for detection of cancer associated dermatomyositis. Besides, they also found paucity of routine myositis antibodies (i.e. antibodies against Jo-1, U1-RNP, U3-RNP, Ku and PM-Scl) in cancer associated myositis patients, quantified as a 6-7 fold increased relative cancer risk in individual lacking 'routine antibodies' compared with those possessing such antibodies. The comprehensive Myositis-specific Antibody test panel incorporating the anti-155/140 antibody however is not widely available in the market yet.

Treatment of the cutaneous and muscle inflammation in paraneoplastic dermatomyositis is of no different from other subtypes of dermatomyositis. Oral prednisolone was the mainstay of treatment in our series and we have used azathioprine, methotrexate and cyclophosphamide as adjunctive treatment. There was concern about whether the use of immunosuppressive therapies would predispose the patient to an increased risk of cancer or promote the advancement of malignancies[22]. This effect has not been proven in the literature and is less likely in our series as most cancers are diagnosed within the first 6 months of the diagnosis of dermatomyositis. The immunosuppressive agents are in fact crucial in the immediate management of dermatomyositis because the disease itself could be life threatening if the myopathy involves the respiratory muscle.

The ultimate treatment of paraneoplastic dermatomyositis is to remove the primary neoplasm. This will result in the resolution of dermatomyositis in most cases. The return of dermatomyositis often indicate the relapse of underlying malignancy and hence paraneoplastic. Malignancy-associated dermatomyositis has a poor prognosis[23]. In our series the fatality in the first year of the diagnosis of dermatomyositis was 33.3% with the overall mortality of at least 38.9%. We have a defaulter rate of 33.3% in the paraneoplastic dermatomyositis series and we were not sure the actual outcome of them. Cancer significantly decreases survival, as one study found patients with DM and malignancy had a 5-year survival of only 10%[15].

CONCLUSION

The strong relationship of adult onset dermatomyositis and malignancy is demonstrated in the current cohort. High vigilance is needed when the clinicians manage them. Investigations for cancer should be guided by clinical signs and symptoms after thorough history and examination. Although the associated malignancies in dermatomyositis may differ with age, gender and regions, nasopharyngeal carcinoma is especially high in our cohort. In the absence of any clues, otorhinolaryngologic evaluation and even a

Table II: Paraneoplastic dermatomyositis (DM) in various countries

Study	No. of Cases of all DM	% of DM a/w malignancy	Commonest cancer associated with DM (%)	Commonest Cancer By country Male	Female
Leow & Goh 1997 *(Singapore)*[4]	38	31.6	NPC (38.4%)	Colo-rectum[28] NPC (6)	Breast[28] Colo-rectum
Chen *et al* 2001 *(Taiwan)*[10]	147	18.0	NPC (22.2%)	Liver[31] NPC (4)	Uteri cervix[31] Breast
Marie *et al* 1999 *(France)*[7]	79	20.3	Colon (31.3%)	Prostate[27] Colo-rectal	Breast[27] Colo-rectal
Hill *et al* 2001 *(Sweden, Denmark & Finland)*[13]	618	32.0	Ovary (11.3%)	Lung[26] Large bowel	Breast[26] Ovary (6)
Stockton *et al* 2001 *(Scotland)*[14]	286	27.0	Lung (32.5%)	Lung[32] Colorectal	Breast[32] Lung
Wakata N *et al* 2002 *(Japan)*[15]	28	36.0	Uterus (20%) Lung (20%)	Stomach[30] Lung	Stomach[30] Breast
Mebazaa A *et al* 2003 *(Tunisia)*[12]	130	15.4	Breast (35%) NPC (25%)	Lung[29] Bladder	Breast[29] NHL
Zhang W *et al* 2009 *(Guangzhou, China)*[16]	678	17.0	NPC (51.3%)	Lung[24] NPC (3)	Breast[24] NPC (5)
Huang YL *et al* 2009 *(Taiwan)*[17]	1059	12.8	NPC (29.2%)	Liver[31] NPC (4)	Uteri cervix[31] Breast
HKL, Malaysia 2009	38	47.4	NPC (61.1%)	Lung[25] NPC (2)	Breast[25] Cervix-uteri

NPC – Nasopharyngeal carcinoma; NHL – Non Hodgkin Lymphoma

Table III: Risk Factors of Malignancy in the series of patients with DM and/or Polymyositis

Study	No of cases	Frequency of cancer %	Risk Factors
Manchull *et al* 1985 *(Toronto)*[5]	71	21	Age > 40 years old
Cox *et al* 1990 *(UK)*[9]	53	43	Increasing age
Basset-Seguin N *et al* 1990 *(France)*[4]	32	41	Elevated ESR, cutaneous necrosis
Leow & Goh 1997 *(Singapore)*[3]	38 DM	31.6	Age > 40 years old
Marie *et al* 1999 *(France)*[7]	79	20	Age > 65 years old, presentation with DM
Pautas *et al* 2000 *(France)*[8]	42	17	Age > 65 years old
Chen *et al* 2001 *(Taiwan)*[10]	147	13	Age > 45years, male sex
Sparsa *et al* 2001 *(Switzerland)*[11]	40	40	Rapid onset of DM/PM, constitutional symptoms, Elevated ESR, high serum creatine kinase levels, No Raynaud phenomenon
Stockton *et al* 2001 *(Scotland)*[14]	705	12.8	Age > 45 years old for DM
Wakata N *et al* 2002 (Japan)[15]	28 DM	36	Male sex, age > 50 years old
Andras C *et al* 2008 *(Hungary)*[34]	309	12	More severe skin lesions and diaphragmatic muscle involvement; Lower creatine kinase and lactate dehydrogenase elevations

ESR – erythrocyte sedimentation rate; DM – Dermatomyositis

blind biopsy of the fossa of Rossenmuller should be considered. Tumour markers were not helpful in the early diagnosis of malignancy. The definitive treatment of paraneoplastic dermatomyositis is to remove the underlying malignancy.

REFERENCES

1. Callen JP, Wortmann RL. Dermatomyositis. Clinics Dermatol. 2006; 24: 363-373.
2. Santmyire-Rosenberger B, Dugan EM. Skin involvement in dermatomyositis. Curr Opin Rheumatol. 2003; 15:714-722.
3. Leow YH, Goh CL. Malignancy in adult dermatomyositis. International J Dermatol. 1997; 36: 904-907.
4. Basset-Seguin N, Roujeau JC, Gherardi R *et al.* Prognostic Factors and Predictive signs of Malignancy in Adult Dermatomyositis, A Study of 32 cases. Arch Dermatol 1990;126(5):633-637.
5. Manchul LE, Pritchard KJ, Tenenbaum J *et al.* The frequency of malignant neoplasms in patients with polymyositis-dermatomyositis. Arch Intern Med 1985; 145:1835-1839.
6. Sigurgeirsson B, Lindelo¨f B, Edhag O, Allander E. Risk of cancer in patients with dermatomyositis or polymyositis. A population-based study. N Engl J Med 1992; 326: 363-367.
7. Marie I, Hatron PY, Levesque H *et al.* Influence on age on characteristics on dermatomyositis and polymyositis in adults. Medicine (Baltimore) 1999;78:139-147.
8. Pautas E, Cherin P, Piette JC *et al.* Features of polymyositis and dermatomyositis in the elderly: a case control study. Clin Exp Rheumatol 2000;18;241-244.
9. Cox NH, Lawrence CM, Langtry JA, Ive FA. Dermatomyositis: disease associations and evaluation of screening investigations for malignancy. Arch Dermatol 1990;126:61-65.
10. Chen YJ, Wu CY, Shen JL. Predicting factors of malignancy in dermatomyositis and polymyositis: a case-control study. Br J Dermatol 2001;144:825-831.
11. Sparsa A, Liozon E, Herrmann F *et al.* Routine vs Malignancy Search for Adult Dermatomyositis and Polymyositis, A study of 40 patients. Arch Dermatol 2002; 138:885-890.
12. Mebazaa A, Boussen Hamouda, Nouira R *et al.* Dermatomyositis and malignancy in Tunisia: A multicenter national retrospective study of 20 cases. J Am Acad dermatol 2003;48:530-534.
13. Hill CL, Zhang Y *et al.* Frequency of specific cancer in patients with dermatomyositis: a population based study. Lancet 2001; 357:96-100.
14. Stockton D, Doherty VR, Brewster DH. Risk of cancer in patients with dermatomyositis or polymyositis, and follow up implications: a Scottish population-based cohort study. Br J Cancer 2001; 85: 41-5.
15. Wakata N, Kurihara T, Saito E, Kinoshita M. Polymyositis and dermatomyositis associated with malignancy: a 30-year retrospective study. Int J Dermatol 2002;41:729-734.
16. Zhang W, Jiang SP, Huang LW. Dermatomyositis and malignancy: a retrospective study of 115 cases. Eur Rev Med Pharmacol Sci 2009; 13(2): 77-80.
17. Huang YL, Chen YJ, Lin MW *et al.* Malignancies associated with dermatomyositis and polymyositis in Taiwan: a nationwide population study. Br J Dermatol 2009; 10.1111/j.1365-2133.2009.09274.
18. Uchiyama T, Arai K, Yamamoto-Tabata T *et al.* Generalized myositis mimicking polymyositis associated with chronic active Epstein–Barr virus infection. J Neurol 2005; 252:519-525.
19. Hashimoto Y, Nawata Y, Kurasawa K *et al.* Investigation of EB virus and cytomegalovirus in rapidly progressive interstitial pneumonitis in polymyositis/dermatomyositis by in situ hybridization and polymerase chain reaction. Clin Immunol Immunopathol 1995; 77:298-306.
20. Kaji K, Fujjimoto M, Hasegawa M *et al.* Identification of a novel autoantibody reactive with 155 and 140kDa nuclear proteins in patients with dermatomyositis: an association with malignancy. Rheumatology 2007;46(1):25-28.
21. Chinoy H, Fertig N, Oddis CV *et al.* The diagnostic utility of myositis autoantibody testing for predicting the risk of cancer-associated myositis. Ann Rheum Dis 2007; 66:1345-1349.
22. Callen JP. Dermatomyositis. Lancet 2000;355:53-57.
23. Danko K, Ponyi A, Constantin T, Borgulya G, Szegedi G. Long term survival of patients with idiopathic inflammatory myopathies according to clinical features: a longitudinal study of 162 cases. Medicine (Baltimore) 2004;83:35-42.
24. Cao KJ, Fan QY, Liu YL *et al.* Cancer incidence and mortality in Guangzhou City from 2000-2002. Ai Zheng 2008: 27(3): 225-30.
25. GCC Lim, Y Halimah. Second Report of the National Cancer Registry. Cancer Incidence in Malaysia 2003.
26. Black RJ, Bray F, Parkin DM. Cancer Incidence and Mortality I the European Union: Cancer Registry Data and Estimates of National Incidence for 1990. Eur J Cancer1997: 33;1075-1107.
27. Colonna M, Danzon A, Delafosse P *et al.* Cancer prevalence in France: Time trend, situation in 2002 and extrapolation to 2012. Eur J Cancer 2008:44; 115-122.
28. Chia KS, Du WB, Sankaranarayanan R *et al.* Population-based cancer survival in Singapore, 1968 to 1992: An overview. Int J Cancer 2001:93(1);142-147.
29. El-Attar IA. Cancer Database in the Arab World. Ethnicity & Disease 2005:15; S1-3 – S1-3.
30. The Research Group for Population-based Cancer Registration in Japan. Cancer Incidence in Japan, 1985-89: Re-estimation Based on Data from Eight Population-based Cancer Registries. Jpn J Clin Oncol 1998:28(1);54-67.
31. Chen CJ, You SL, Lin LH. Cancer Epidemiology and Control in Taiwan: a Brief Review. Jpn J Clin Oncol 2002: 32 (Supp); S66-S81.
32. Scottish Executive. Cancer in Scotland: Sustaining Change: Cancer Incidence Projections for Scotland (2001-2020) - An aid to planning cancer services. ISD Epidemiology and Statistics Group, NHS National Services Scotland, August 2004.
33. Amoura Z, Duhaut P, Huong DLT *et al.* Tumor Antigen Markers for the Detection of Solid Cancers in Inflammatory Myopathies. Cancer Epidemiol Biomarkers Prev 2005; 14(5):1279-1282.
34. Andras C, Ponyi A, Constantin T *et al.* Dermatomyositis and polymyositis associated with malignancy: a 21-year retrospective study. J Rheumatol 2008;35(3):438-444.