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Contents

PAEDIATRIC DERMATOLOGY - Review Article

Recognising cutaneous signs and the management in paediatric connective tissue diseases

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Keywords *Juvenile systemic lupus erythematosus, juvenile dermatomyositis treatment*

Introduction

Paediatric rheumatology is an emerging field in paediatrics which deals with both inflammatory and non inflammatory conditions of the connective tissue and joints in children. In paediatric rheumatology, the skin remains one of the most important organs which can be involved especially with respect to the group of inflammatory connective tissue diseases. In children with these diseases, the cutaneous signs are often important diagnostic clues of the underlying disease.

However, due to the rarity of these conditions and the relative inexperience by many, these cutaneous signs can sometimes be mistakenly diagnosed. This not only leads to a delay in diagnosis but also institution of appropriate therapy and a detrimental long term outcome. In this review, the focus will be on cutaneous signs in the two main paediatric connective tissue disorders and its current management.

Juvenile Systemic Lupus Erythematosus (JSLE)

Juvenile systemic lupus erythematosus (JSLE) or childhood lupus is a chronic multisystem autoimmune disease that accounts for 15-20% of all lupus patients. In the paediatric population, cutaneous manifestations remain one of the common organ systems to be involved and are present in an estimated 50-80% of children at initial presentation[1]. In a Malaysian study of 38 children with JSLE, 89% had cutaneous symptoms and signs at initial presentation of which only 55% had malar rash, 45% mucosal ulceration and 42% alopecia[2].

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Cutaneous involvement in JSLE can be either due to lupus specific interface dermatitis or non specific manifestations of lupus like (photosensitivity, vasculitis, erythema or Raynaud's phenomenon). Lupus specific cutaneous disease can be further divided into acute cutaneous lupus, subacute cutaneous lupus (SCLE) and chronic cutaneous (discoid) lupus (CCLE). As a result of this, the presentation of skin disease in lupus can be very varied. Whilst lupus specific skin lesions serve primarily as an important diagnostic clue to the underlying disease, the presence non specific lupus lesions has been associated with more active SLE and hence may warrant more intensive therapy and disease monitoring[3].

The malar rash or 'butterfly' rash which is the typical rash of SLE unfortunately only occurs in about 50-70% of childhood lupus. One needs to remember that although it is pathognomonic of SLE, it is not a diagnostic rash and can be present in other conditions like juvenile dermatomyositis. Subacute cutaneous lesions are rare in children and often begin as papules that evolve to annular lesions with raised edges which can then crust, become hyperpigmented and atrophied. Discoid skin lesions are also relatively rare in children and characterized by sharply demarcated papulosquamous lesions which are often photosensitive and heal with atrophy and scarring. It is important to note that discoid lesions in children tend to have a higher chance of being associated or transitioning to systemic lupus erythematosus as compared to adults, and hence a careful search for systemic symptoms is warranted once a diagnosis of discoid LE is made[4]. Children with lupus can also present with various non specific rashes like maculopapular rashes, petechiae, purpura or urticaria. The fingers and nails need to be checked carefully looking for nailfold infarcts and periungual erythema. Periungual erythema which is the result of nail fold capillary dilatation and tortuosity is not a finding which is specific to lupus and can be found in other connective tissue diseases like juvenile

dermatomyositis, juvenile scleroderma and undifferentiated connective tissue disease. In lupus, nailfold capillary abnormalities appear to be related to disease activity as well as the presence of various different autoantibodies like anti-cardiolipin, anti-Sm and also the presence and higher titres of anti-dsDNA antibodies[5]. Livedo reticularis is also sometimes seen in children and one needs to investigate for associated presence of antiphospholipid antibodies[6]. Diffuse alopecia is common in active lupus while scarring alopecia is not common in children. Rare presentations include vesicobullous lesions, nodules, lupus profundus and chilblain lupus. Oral mucosal lesions are also common and there can either be palate erythema or classically a shallow, ragged painless ulcer on the hard palate. On some occasions, there can also be nasal septum ulceration.

As in adult patients, skin disease can sometimes be one of the most refractory clinical manifestations of JSLE. The standard therapy consists of sun protection, topical corticosteroids and antimalarials. In addition, children are advised to avoid direct sun exposure, wear lightweight tightly woven clothing and use broad-spectrum, water resistant sunscreens. Sun avoidance in particular is difficult for children and ensuring compliance is a challenge as this often limits their physical activities or play especially at school or with friends. In addition, children generally do not like applying sunscreens for reasons of stickiness, smell or colour especially in those who have pigmented skin. Skin lesions of acute LE often resolve with treatment of the systemic disease in particular the addition of oral steroids but management of more persistent skin lesions remain a challenge. Some additional suggested treatments include methotrexate, intravenous immunoglobulin, mycophenolate mofetil and more recently anti-CD 20 monoclonal antibody rituximab.

Low dose methotrexate given in weekly dosages has been reported in various uncontrolled case series to be of benefit for adults with active cutaneous and/or articular disease[7,8,9]. However the efficacy of methotrexate for skin disease in the paediatric population is not so clear with two studies yielding conflicting results. Abud- Mendoza et al treated 10 children with various manifestations including 7 with cutaneous symptoms and found in this group, positive response in 80% (5 excellent, 3 good) with only 1 patient having a poor response[10]. However Ravielli et al in his cohort of 11 paediatric onset lupus of which majority had nephritis, found no response for the cutaneous symptoms (3 malar rash and 2 skin vasculitis) and also that methotrexate did not show any major corticosteroid sparing potential[11].

Mycophenolate mofetil (MMF), an immunosuppressive agent initially used for transplantation has proven to be beneficial in lupus nephritis in both adults and children. However the evidence for refractory skin disease has been conflicting. Several adult case reports and case series have shown good response to MMF and this included patients with refractory discoid lupus, SCLE, lupus profundus, lupus pernio, lupus tumidus and chilblain lupus[12, 13, 14, 15]. However in another adult case series of 7 patients who had previously failed to respond to a median of 4 drugs, response to MMF was poor with only one patient showing a partial response and another showing an initial response but flared subsequently even whilst on MMF[16]. Currently, most available MMF data in children relates to its efficacy as either an induction or maintenance agent for lupus nephritis but there is suggestion that MMF may be of benefit especially in non-renal lupus although there are no specific reports on the response of refractory cutaneous disease in children[17,18,19].

Rituximab, a chimeric monoclonal anti-CD20 IgG1 antibody has shown promising results in paediatric patients with severe or refractory SLE mainly involving lupus nephritis, severe vasculitis or cytopenias[20, 21]. There is inadequate experience of its use in isolated skin disease. There is a recent case report of successful use of rituximabf[22] or refractory lupus skin disease in an adult. An 11 year old paediatric patient with recurrent skin flares with systemic manifestations has also been successfully treated with rituximab and remained in remission 9 months after initiating therapy[23].

Oral thalidomide has also been reported to be a very useful agent in inducing remission for refractory lupus skin lesions in adults but its use is limited by potential teratogenicity as well as peripheral neuropathy[24,25,26]. Although the response may be good, the effect of thalidomide appears not to be sustained and a relapse rate of as high as 67% was reported upon cessation of the drug in one study[26]. In children, data on thalidomide is scarce and is currently reserved only for those with severe

autoimmune pathologies. A major difficulty concerning the use of thalidomide in children is the monitoring for peripheral neuropathy. The peripheral neuropathy unlike in adults, has been shown to be dose-dependent especially cumulative dosages; age dependent and also occurs at a significantly high frequency of 53.8%, and thus has to be used with much caution[27]. Children may not be able to verbalise symptoms of clinical neuropathy and it is difficult to perform nerve conduction test in small children frequently. There is promise of safer thalidomide analogues on the horizon which may then make this an appropriate choice in the future.

Topical pimecrolimus 1% cream, an ascomycin macrolactam which inhibits calcineurin and has no atrophogenic potential has been reported to be safe and efficacious in small cases series in adults but no available data in children[28,29].

In our experience managing childhood lupus, most cutaneous lesions respond to topical corticosteroids, antimalarials and sometimes require low dose prednisolone. However second line agents like methotrexate and azathioprine do not seem to have beneficial effects in improving refractory skin lesions. Intravenous immunoglobulin has been tried in 3 patients with refractory cutaneous symptoms but we did not see any improvement. Mycophenolate mofetil has been used successfully in two patients with chronic discoid lupus with skin vasculitis - one who had previously failed oral prednisolone and monthly intravenous pulse methylprednisolone, antimalarials, azathioprine, intravenous immunoglobulin and 6 months of intravenous cycophosphamide. The other had failed antimalarials, azathioprine and six months of monthly intravenous immunoglobulin. The improvement in the skin rash was seen as early as 2 months after initiation of MMF therapy. Currently, Rituximab has been reserved for children with more severe major organ involvement of lupus.

Juvenile Dermatomyositis

Juvenile Dermatomyositis (JDM) is a rare disease but remains the commonest of all the idiopathic inflammatory myopathies of childhood. It characteristically affects the proximal muscles resulting in weakness and also the skin with pathognomonic rashes. However, the cutaneous disease does not always parallel the muscle disease in terms of onset, activity or response to therapy. Although both these organ systems can be affected simultaneously at presentation, at times the manifestation of one organ system may precede the other and often the skin rashes may be undiagnosed for months before the clinical muscle weakness sets in. In an unpublished study of 20 Malaysian children with JDM, the initial presentation in 50% of the patients was cutaneous alone with only 20% presenting simultaneously with skin rashes and muscle disease. In this cohort, facial rash was the commonest presentation present in 90% of the patients whilst Gottron papules was reported in 75% of patients. The mean delay between onset of skin disease to diagnosis was 15 months indicating a significant delay in diagnosis[30].

Juvenile dermatomyositis has typical skin rash which include the heliotrope rash and Gottron papules. Heliotrope rash is a purplish discolouration of the upper eyelids whilst Gottron papules are erythematous scaly lesions often found over the metacarpophalangeal and proximal interphalangeal joints as well as over the elbows and knees. In our experience, the Gottron papules may sometimes just be non-discrete erythema and often in our population especially those with pigmented skin, the rash can appears as non-erythematous hyperpigmented lesions. Lesions over the elbows are more common than over the knees and Gottron papules are also seen on occasions over the distal interphalangeal joints although it is usually associated with lesions elsewhere. Children with JDM can also present with a malar rash which is often well demarcated although the area of involvement can be quite small and sometimes be missed. In some children, an extensive erythematous rash can also occur over the whole body whilst others can present with vasculitic or ulcerative skin lesions and these often signify a more aggressive disease and a poor prognosis. Periungual erythema due to nailfold capillary loop dilatations is common and can affect both finger and toe tips. In some instances in acute JDM, there can also be periorbital oedema or diffuse oedema of the whole face whether erythematous or not. This is sometimes mistaken as an allergic reaction to various drugs administered. Photosensitivity is also a feature in these patients and sun exposure can precipitate a flare. Calcinosis and lipodystrophy are considered complications of inadequately or prolonged untreated disease.

Smith et al in a study of 60 newly diagnosed, previously untreated children with JDM found that the cutaneous manifestations were associated with end row capillary loss which indicated a vasculopathy. As such, they proposed that the cutaneous manifestations of JDM are associated with vascular disease and hence warrant aggressive therapy[31]. The presence of a persistent rash and the duration of untreated disease have also been associated with one of the dreaded complications of JDM which is calcifications[32]. As such, cutaneous lesions of JDM need to be diagnosed accurately and given prompt and perhaps systemic therapy.

As in JSLE, the standard therapy for skin lesions in JDM include sun protection, topical cortiosteroids and sometimes antimalarials. More resistant skin lesions sometimes require the addition of low dose oral corticosteroids. The use of topical immunosuppressive agents has largely been disappointing. In an unblinded observational study of 5 adults with dermatomyositis and 1 child with JDM, topical tacrolimus was reported to be a useful adjunct in patients for refractory cutaneous lesions[33]. However this beneficial effect was not observed in another study whereby none of the 5 patients treated with topical tacrolimus showed any improvement[34]. Oral tacrolimus on the other hand, has been reported to be of benefit for severe cutaneous manifestations in a total of 9 children in 2 different case series but its role in controlling muscle disease is conflicting in these 2 studies[35,36].

Intravenous immunoglobulin has been proven effective as an adjunctive treatment for myositis in severe JDM with improvement in disease activity as well as permitting steroid reduction[37,38]. In addition, Lang et al also reported 5 children who not only showed improvement in their muscle strength but also their skin rash[39]. Two adult patients treated with intravenous immunoglobulin for their skin disease in dermatomyositis have also been reported to show response - one complete and one partial[40].

Riley et al reviewed the efficacy of intravenous pulse Cyclophosphamide in 12 patients with severe refractory JDM and of these 8 had ulcerative skin lesions. Two patients died of underlying pulmonary insufficiency early in the disease, but the remaining 10 showed improvement after 6 months of treatment in both muscular and extra-muscular disease including skin scores. Although all the ulcerative skin disease was successfully treated, other skin disease was also one of the main persistent features[41].

Other drugs which have been tried include the following. Infliximab has also recently been reported to be of benefit for 5 children with refractory JDM but the positive effect was mainly noted for muscle disease, contractures and calcinosis whilst skin disease was less well controlled[42]. As in JSLE, Rituximab, a chimeric monoclonal anti - CD20 IgG1 antibody has also been reported to be potentially useful for JDM in an observational study of 4 children of which 3 showed clinical benefit regardless of status of myositis specific antibodies[43].

In our experience, monthly intravenous immunoglobulin (IVIg) at 1g/kg/day for 2 days has been used in six children with severe JDM with moderate success. One patient with only severe cutaneous disease who had failed prior therapy with oral and topical corticosteroids, antimalarials, methotrexate and topical tacrolimus showed a dramatic response and went into complete remission only after 2 doses of IVIg and has remained in remission since then. Four other children showed improvement in both their cutaneous and muscle disease whilst one child did not show any response despite having had a prolonged 12 month course of intravenous immunoglobulin. We postulate that the poor response in this child is due to long term damage from uncontrolled inflammation which is irreversible.

Conclusion

The prognosis of common paediatric connective tissue diseases like juvenile systemic lupus erythematosus and juvenile dermatomyositis has improved tremendously over the recent decades with better understanding of the disease as well as more aggressive therapy. However, the treatment for cutaneous manifestations in these diseases has largely remained the same and resistant skin manifestations continue to be a therapeutic challenge. The emergence and ongoing research of new drugs including biologic therapy have offered promise in these situations but more research has to be conducted before they can be widely applied especially in children.

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DERMATO-ONCOLOGY - Original Article

Pattern of cutaneous malignancies in a tertiary hospital in Sarawak

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Abstract

Background Most Asian studies have determined that basal cell carcinoma (BCC) is the commonest skin cancer followed by squamous cell carcinoma (SCC), malignant melanoma (MM) and others. The pattern of cutaneous malignancies has never been determined in Sarawak. Thus, this retrospective study was performed to determine the pattern among patients attending the skin clinic in Sarawak General Hospital.

Materials and Methods The clinic notes of 87 patients diagnosed to have skin cancer histopathologically between 2000 and 2008 were retrieved and subjected to descriptive analysis. Analysis for the pattern of disease and demographics was performed.

Results BCC constituted the main skin cancer with 49.4% (n=43) followed by SCC with 26.4% (n=23), cutaneous lymphomas (CL) with 9.2% (n=8), MM with 4.6% (n=4) and other cutaneous malignancies with 10.3% (n=9). The number of cases detected steadily increased over the 8 year period, with most BCC and SCC diagnosed after 2003. The mean age of presentation was highest in patients suffering from SCC at 62.7 years followed by BCC 60.9 years, MM 59 years, CL 54.3 years and other malignancies 40.6 years. Female predominance was noted in all the malignancies except squamous cell carcinoma. Chinese constituted the majority of cases (50.6%) followed by Malays (29.9%), Bidayuhs (9.2%), Ibans (8.0%) and other indigenous people of Sarawak (2.3%). This pattern of distribution corresponds with the racial distribution of the clinic attendance.

Conclusion Cutaneous malignancies in Sarawak differ from regional pattern in that CL is ranked as the third commonest skin cancer and that female predominance was seen in BCC, CL, MM and other skin cancers.

Keywords *skin cancer, pattern of disease, demographics*

Introduction

Cutaneous malignancy is estimated to occur in 20% to 30% of all malignancies in Caucasians, 2% to 4% of all neoplasm in Orientals, and 1% to 2% of all cancers in Africans and Indians[1]. It has been recognized as the most common malignancy among Caucasian population[2,3]. In neighbouring Singapore, skin cancer is ranked seventh in their cancer registry[4].

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Conflict of interest : Nil

Basal cell carcinoma (BCC) is the most common skin malignancy in Orientals, Caucasians, Hispanics[1,4,5]. However, among Indians and Africans, squamous cell carcinoma (SCC) is recognized as the most common skin cancer[6,7].

Malignant melanoma (MM) is seen as the third most common cutaneous malignancy among Asians, Caucasians, Hispanics and Africans[4,7,8]. In Japan, cutaneous T cell lymphoma is seen as the fourth commonest skin malignancy, representing approximately 5% of the skin cancer[9]. Kaposi's sarcoma is seen as a common cancer in Africans, representing around 10% of their cancer load[10]. The pattern of skin cancer in Sarawak has never been reported. Sarawak is unique as it is inhabited by the native tribes. In Kuching where the Sarawak

General Hospital is situated, Bidayuhs and Ibans are the major ethnic tribes served. Skin clinic in Sarawak General Hospital is the only skin referral centre for the whole state of Sarawak. This tertiary centre caters mainly for the Chinese, Malays, Bidayuhs and Ibans. A retrospective study is undertaken to determine the pattern of skin malignancy seen in the Sarawak General Hospital between 2000 and 2008.

Materials and methods

All the clinic cards of patients attending skin clinic, Sarawak General Hospital between 2000 and 2008 were searched. Of these, 87 patients were diagnosed to have cutaneous malignancy histopathologically. Demographic data and type of malignancy were recorded. The data collected was subjected to descriptive analysis. The analysis was done for the pattern of the skin cancer seen and presented as the percentage of each type of cancer. Among each type, demographic data regarding age, sex, race and occupation were described. The occupation described in this study is divided into those who are frequently sun exposed e.g. farmers and construction workers or those who are not sun exposed e.g. clerk, administrators and housewives. This is to determine whether the cancer recorded has any relevance to sun exposure.

Results

Between 2000 and 2008, 87 patients were diagnosed to have cutaneous malignancies. Of these, 49.4% (n=43) had BCC, 26.4% (n=23) had SCC, 9.2% (n=8) had cutaneous lymphomas (CL), 4.6% (n=4) had MM and 10.3% (n=9) had other cutaneous malignancies. For patients diagnosed with CL, we observed that 50% (n=4) had mycosis fungoides, 25% (n=2) cutaneous B cell lymphoma, 12.5% (n=1) cutaneous T cell lymphoma and 12.5% (n=1) anaplastic large cell lymphoma. For patients diagnosed to have other cutaneous malignancies, we noted that 66.7% (n=6) had metastases from other malignancy (1 acute myeloid leukemia, 1 chronic myeloid leukemia, 1 lung carcinoma, 1 breast cancer, 1 nasopharyngeal cancer and 1 colonic cancer) and 33.3% (n=3) had dermatofibrosarcoma protuberans. Figure 1 shows the type of malignancies diagnosed by year. It shows that cutaneous malignancies were steadily increasing over the 8 year period. Most of the malignancies especially BCC and SCC were diagnosed from 2004 onwards.

Figure 1 Cutaneous Malignancies in Sarawak General Hospital (n-87)

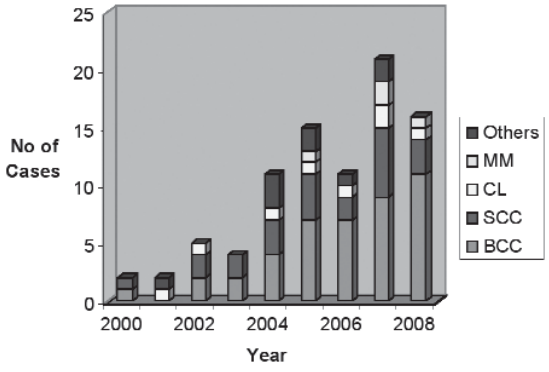

Table 1 Demographics of cutaneous malignancies in Sarawak General Hospital

	BCC (n=43)	SCC (n=23)	CL (n=8)	MM (n=4)	Others (n=9)
Mean age (yrs)	60.9	62.7	54.3	59.0	40.6
Female sex	22 (51.2%)	9 (39.1%)	7 (87.5%)	3 (75.0%)	7 (77.8%)
Occupations with sun exposure	15 (34.9%)	4 (17.4%)	0	0	0
Race					
Chinese	19 (44.2%)	13 (56.5%)	3 (37.5%)	3 (75.0%)	6 (66.7%)
Malay	14 (32.6%)	10 (43.5%)	1 (12.5%)	1 (25.0%)	0
Bidayuh	6 (14.0%)	0	1 (12.5%)	0	1 (11.1%)
Iban	3 (6.9%)	0	3 (37.5%)	0	1 (11.1%)
Others	1 (2.3%)	0	0	0	1 (11.1%)

Table 1 shows the demographic data of patients with various cutaneous malignancies. We observed a female predominance in all the malignancies except squamous cell carcinoma. Among patients diagnosed with MM, CL and other malignancies, more than 75% were female. The mean age of presentation was highest in patients suffering from SCC with 62.7 years (range, 33 to 85 years) followed by BCC with 60.9 years (range, 35 to 83 years); MM with 59 years (range, 40 to 75 years); CL with 54.3 years (range, 28 to 89 years) and other malignancies with 40.6 years (range, 18 to 58 years). Occupation related to constant sun exposure was observed in 34.9% with BCC and 17.4% with SCC. None of the patients with CL, MM and other cancers had occupation related to constant sun exposure.

Discussion

In Sarawak General Hospital, we noted that BCC is the commonest skin cancer followed by SCC, CL and MM. In Singapore, Koh et al also noted that BCC was the commonest skin cancer in their study followed by SCC. However, they noted that MM was ranked third[4]. The differences might be attributed to the ethnicity of the population. Seventy seven percent of Singaporeans are Chinese with Fitzpatrick skin types III and IV, 14% Malays with skin type V and 8% Indians with having skin type VI[4]. In Sarawak, Ibans with skin type V make up 30% of the total population, Chinese 26%, Malays 21% and Bidayuhs with skin type VI and V 10%[11]. Fairer skin Chinese are more prone to have MM than darker skin Indians[4]. Moreover, Caucasians with skin type I and II are 3 to 7 times more prone to develop MM than Hispanics with skin type II and IV. In turn, Hispanics are 1 to 4 times more prone than blacks with skin type VI and Asians[8,12].

Thus, by having a darker skin complexion, population of Sarawak are more protected from developing MM. Another possibility is that MM is under diagnosed in Sarawak as the acral lentiginous type commonly seen here might be misdiagnosed as other diseases e.g. fungal infection, mole and trauma and never referred to the skin clinic for proper assessment.

The finding of CL as the third commonest skin malignancy in Sarawak is very interesting. The reason for the high incidence of CL of 9.2% and especially in Ibans is unknown. Similarly, the high incidence of mycosis fungoides of 12.1% among blacks is also unknown[7]. Generally mycoses fungoides is seen twice as common in blacks compared to whites[13]. A possible postulate is that the darker skin type that protects against MM allows the expression of CL.

The pattern of primary CL seen in Sarawak corresponds to the pattern seen in the United States. Zackheim et al noted that mycosis fungoides constituted 82.3% of total primary CL cases followed by lymphomatoid papulosis with 9.4%, B cell lymphoma 4.5%, primary T cell lymphoma 2.9% and anaplastic large cell lymphoma 0.9%[14]. In our study, we found that mycosis fungoides was the commonest primary CL seen followed by primary B cell CL, primary T cell CL and anaplastic large cell lymphoma. However, the proportion of patients diagnosed with mycosis fungoides was lower, at only 50%.

In Taiwan, 1.02% of the 12146 patients with internal malignancies had metastasized to the skin[15]. The highest rates of skin metastases were found to occur from carcinoma of the breast, followed by the lung, oral mucosa, colon and rectum, stomach, and esophagus. We also found skin metastases from breast and colon. Interestingly, we also found a patient with skin metastases from nasopharyngeal cancer, one of the commonest cancers in Sarawak.

BCC is commonly seen in males with a male to female ratio of 2: 1[16]. In Australia, the incidence of BCC in those aged under 40 is higher in women than men, after which rates in men exceed women[17]. However, our study showed the ratio of both sexes was almost equal. In Singapore, Koh et al also noted an almost equal incidence of BCC among the predominant Chinese and Malay population[4]. In SCC, the male to female ratio was between 1.5 and 1.9 among the Singaporean Chinese[4]. Here, we noted that the ratio was 1.6. CL is more common in males with a ratio of 2:1[18]. MM has almost equal sex distribution among Japanese but more common in males among Singaporean Chinese[4,9]. In Sarawak, we noted that both these conditions were more common in females. Nevertheless, the number of patients in this study is small and might not be representative of the population in the whole state.

Cutaneous malignancies are increased in individuals with total, occupational, and recreational sun exposure. Those with total and occupational sun exposure are at increase risk of having SCC while those with recreational exposure have higher risk of MM and BCC[19]. The nature of ultraviolet (UV) radiation exposure responsible for BCC is unclear[16]. However, it is noted that the risk of BCC is associated with ease of sun burning especially during childhood[16]. High cumulative UV exposure is only related to SCC. It is expected that most of the patients with SCC will be working and spending most of their time under the sun. However, we only noted that 17.4% of our patients with SCC had occupation related to constant sun exposure.

This might indicate that living in the tropics, without working constantly under the sun, increases the individual risk to skin cancer. This study is limited by its retrospective nature and the small number of patients. Analysis of CL, MM and other skin cancers were affected mainly by the small number of patients with these malignancies.

In conclusion, cutaneous malignancies in Sarawak differ from regional pattern in that CL is ranked as the third commonest skin cancer. In addition, female predominance was seen in BCC, CL, MM and other skin cancers in Sarawak.

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AUTOIMMUNE DISORDERS - Original Article

Henoch - Schönlein Purpura: Relationship between cutaneous clinical manifestations with severity outcomes: A 5-year retrospective study

Tarita T, M Med, Lee CE, MBBS, Rohna R, MRCP

Abstract

Background Henöch - Schonlein Purpura (HSP) is an Immunoglobulin A-mediated systemic small vessel vasculitis of childhood and adults. HSP usually presents with a classical tetrad of rash, polyarthralgia, abdominal pain, and renal disease. Complications may arise from vasculitis of systemic organs.

Objectives The purpose of the study was to determine the clinical patterns of HSP and whether the cutaneous clinical manifestations of HSP can prognosticate the severity outcome of the disease.

Methodology We conducted a retrospective study of all patients diagnosed with HSP by dermatologists in Selayang Hospital between January 2003 and December 2007. The data were obtained from the case records and analyzed with regard to age, sex, race, associated triggering factors, cutaneous clinical symptoms and signs, associated systemic clinical features and systemic complications.

Results There was a total of 50 patients during this period. HSP was diagnosed more in adults than children. Fifty-four percent of patients were of Malay origin. The mean age at presentation for children was 6.6 years and 31 years for the adult group. There was an overall female preponderance in adults HSP. Majority (48%) of patients presented within 1 week of the onset of symptoms. The purpuric rashes were distributed on the trunk in 20% of cases, and on the upper limbs in 56% of cases. Vasculitic ulcer was part of the clinical features in 4% of cases while vasculitic blisters in 12%. There was a significant association (Fisher Exact Test, $p = 0.02$) and correlation (Pearson, $p = 0.03$) between the extent of skin involvement with gastrointestinal haemorrhage in the former and renal involvement in the latter. There was no significance association between vasculitic blisters or ulcer with the disease severity outcomes. There was no significant difference of cutaneous presentation with regards to the triggering factors of the disease.

Conclusion The results of our retrospective study demonstrated that the cutaneous clinical presentation is one of the predictive factors of renal and gastrointestinal outcomes in HSP. There was a female preponderance among HSP in adults patients with a low occurrence of articular syndromes

Keywords *Henoch Schönlein Purpura, Leucocytoclastic Vasculitis*

Introduction

Henoch - Schonlein Purpura (HSP) is an Immunoglobulin A- mediated systemic vasculitis of childhood and adults. Complications arise from vasculitis of systemic organs. The long-term morbidity of HSP is predominantly attributed to renal involvement, while the short term morbidity is mainly attributed to gastrointestinal complication.

The rash, which occurs in all patients, is characterized clinically as palpable purpura. The lesions are typically nonblanching, as they represent extravasation of blood into the skin, and

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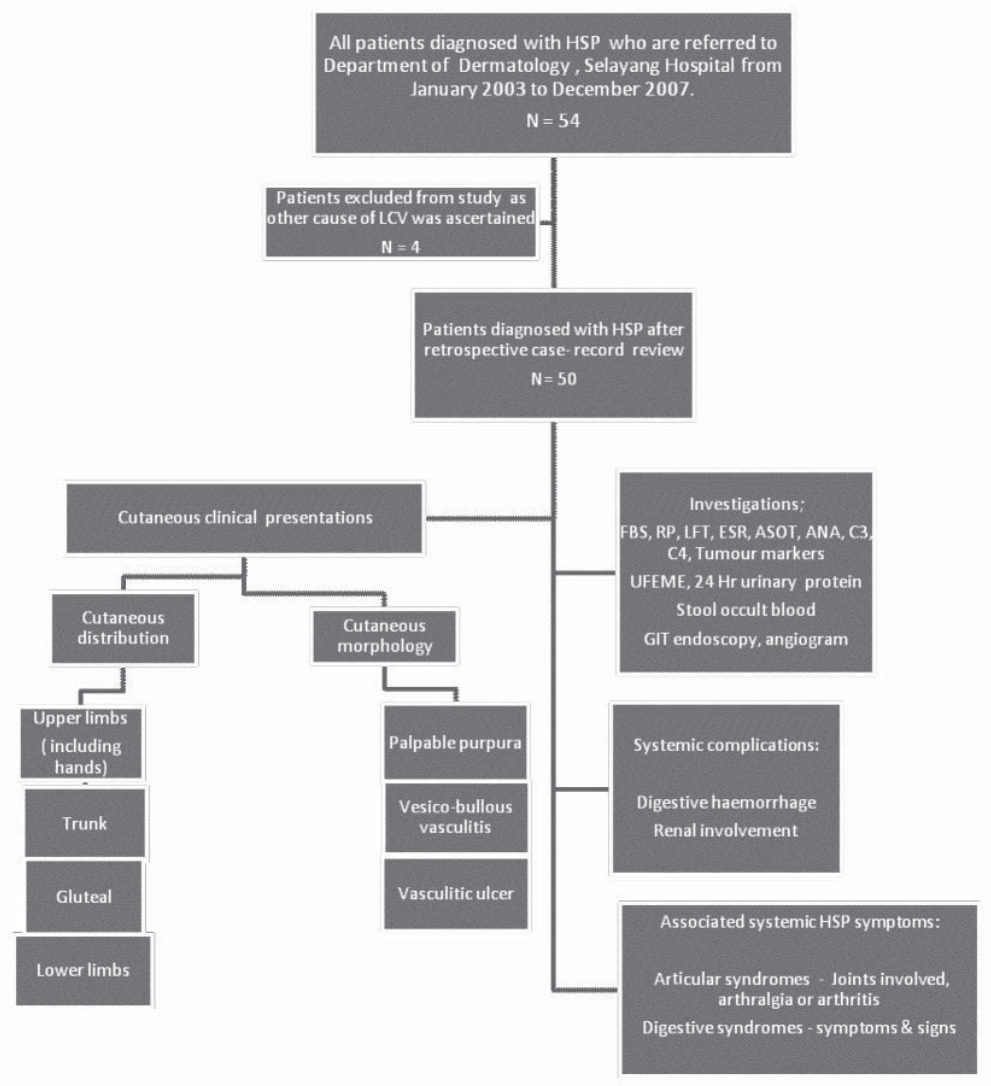
they often occur in groups that can persist for 3 to 10 days[1]. They can occur anywhere on the skin but are often concentrated on the lower legs and arms. These vasculitic rashes may manifest with ulcer and vesico-bullous lesions. In children, local angioedema may precede the development of the purpura. Other cutaneous manifestations include skin oedema, urticaria and erythema multiforme.

The clinical manifestations of HSP are a consequence of widespread leukocytoclastic vasculitis (LCV) with IgA deposition in vessel walls. IgA deposition in the renal mesangium causes nephritis in some patients. HSP is associated with abnormalities involving IgA1 alone, but not IgA2. Pathogenesis may due to abnormalies in glycosylation of IgA1 and IgA1-receptor interactions[2]. The histopathology reveals subepidermal hemorrhages, necrotizing vasculitis of the small vessels of the dermis with IgA & C3 deposition.

Figure 1 Flow-chart of the study work-process



Adult HSP is infrequently reported in adults over the age of 20, is characterized by a lower frequency of abdominal pain and fever, and a higher frequency of joint symptoms, and renal involvement which tend be severe[3,4,5,6]. It has been reported that the spread of purpura to the trunk apart from other clinical factors; a recent infectious history, pyrexia, the spread and biologic markers of inflammation, are predictive factors for renal involvement[7]. We aim to study the clinical patterns of HSP referred to the Dermatology Department, Selayang Hospital, Malaysia and to determine whether the cutaneous clinical signs could prognosticate the severity outcomes of the disease.

Materials and methods

This study was conducted in a retrospective - cohort manner after research and ethical approval.

It included all patients with HSP who were diagnosed by dermatologists in Selayang Hospital over a 5-year period, from January 2003 till December 2007. The diagnosis was established clinically in the presence of cutaneous syndrome with symmetrical declivitous region non-thrombocytopenic purpura. The study group was selected by universal sampling, from the department records which concluded the in-patient and out-patients census. Further data was abstracted from the Cerner system incorporated in Selayang Hospital medical-services computers. A retrospective review of records had eliminated a few patients diagnosed with vasculitis syndromes which mimicked HSP at initial presentations (Figure 1).

Details of information which was collected included the demographic data, associated triggering factors, cutaneous clinical symptoms and signs, associated systemic clinical features, related laboratory investigations and systemic complications. The non - parametric variables gathered included the following; age, duration at presentation, haematuria, protenuria, 24 Hour-urinary protein, hemoglobin and anti-Streptolysin O Titre. Under categorical data were sex, race, stool occult blood, skin morphology, skin distribution and HSP trigger factors.

The data findings were analyzed using SPSS (version 14.0) statistical analysis software. The Fisher's exact test was used for univariate analysis, and multiple logistic regression for multivariate analysis. Bivariate linear correlations are used with numerical data. The null hypothesis postulated were as following; 1) there is no relation between cutaneous manifestation of HSP and the severity of the disease, 2) there is no relation between the disease cutaneous manifestation and the various HSP triggering factors.

Abbreviations

- FBC full blood count
- RP renal rofile
- LFT liver function test
- ESR erythrocyte sedimentation rate
- ASOT anti-streptolysin O titre,
- C3 complement factor 3,
- C4 complement factor 4,
- ANA antinuclear antibody,
- UFEME urine full examination and microscopic examination,
- GIT gastrointestinal
- UFEME urine full examination and microscopic examination,
- GIT gastrointestinal

Results

Over the 5-year period, a total 50 patients were diagnosed with HSP of whom 27 (54%) were female and 23 (46%) male. The age at presentation ranged between 4 to 65 yrs old (overall mean 31 $\pm$ 17). Among the children who comprised 10% of the study patients, the mean age at presentation was 6.2 years, whereas in adults it was 31 years old.

Overall, 90% of patients were adults. There was male preponderance in the children group with a male to female ratio of 1.5:1 and a female preponderance in the adult group with a female to male ration of 1.25: 1. Majority of patients (26%) seen were within the age category of 21 to 30 yrs old. The racial distribution for all cases of HSP was as follows: 54 % Malay, 28% Chinese, 12% Indian and 6% others (table 1).

Digestive hemorrhage was found in 8 patients and renal involvement of variable severity was found in 38 patients. The age of patients who had digestive haemorrhage is as following; 1 patient aged 6yrs old, 4 patients aged between 20 to 24 yrs-old, 2 aged between 50 to 59 yrs old and 1 aged 64 yrs old. A 32 yr old Malay lady and a 20 yrs old Chinese man had urgent gastrointestinal endoscopy done

Table 1 Baseline demographic characteristics of study patients

Characteristics	Adult (N = 45)	Children < 12yrs old (N = 5)
Age (mean) years	31 (12 - 65)	6.2 (4 - 9) years
Age (years)		
1 - 10	-	5 (10%)
11 - 20	10 (20%)	
21 - 30	13 (26%)	
31 - 40	9 (18%)	
41 - 50	3 (6%)	
51 - 60	7 (18%)	
61 - 70	3 (6%)	
Sex		
Male	20	3
Female	25	2
M: F ratio	0.8: 1	1.5: 1
Race		
Malay	24	3
Chinese	12	2
Indian	6	0
Others	3	0

which demonstrated gut vasculitis. None of the patients reported gastrointestinal angiogram abnormality. 3 children (60% of total children) and a similar percentage of adult patients had renal involvement. Chronic kidney desease secondary to Ig A nehropathy was documented as early as 2 months after disease onset in a 25 year old Indian lady and as late as 4 years in a 33 year old Malay lady. Thirty two percent of patients were documented as HSP post-Sreptococcus infection. HSP was associated with a Gullain Barre Syndrome, infective endocarditis in a case, varicella zoster infection, hepatocellular carcinoma in a case and metastatic mitotic lesions (died of myocardial infarction) (Table 2). Several factors other than streptococcal infection have been known to be associated as triggers of HSP such as *Helicobacter pylori*, various viral agents, foods, drugs, insect bites, vaccinations, exposure to cold and neoplastic disorders.

Quantitative data analysis revealed that there was a significant association (Fisher's Exact Test, p = 0.02) between vasculitic rashes distribution on the trunk and gastrointestinal haemorrhage. Correlation analysis showed significant correlation (Pearson p = 0.03) between distribution of vasculitic rash on hands with renal involvement and also significant correlation (Pearson, p = 0.03) between extent of vasculitic rash on the trunk and upper limbs with renal involvement. Further analysis showed no significant association between cutaneous clinical morphology and the severity outcomes of HSP. There was also no significant difference between the cutaneous clinical presentation of post-*Streptococcus HSP* and non post-*Streptococcus HSP*.

The result of fischer exact test is as follows:

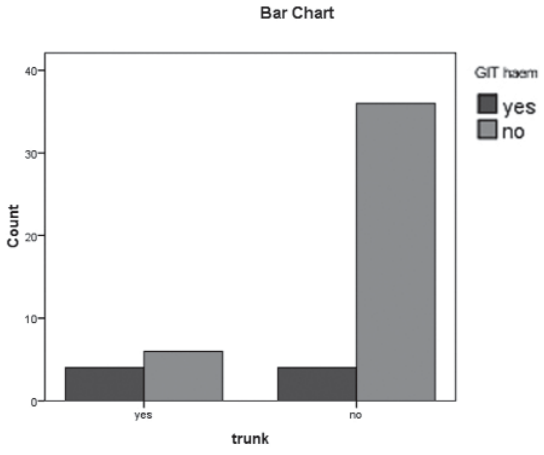
Chi-Square Test

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	5.357[a]	1	.021
Continuity Correction[b]	3.358	1	.067
Likelihood Ratio	4.500	1	.034
Fisher's Exact Test			
Number of Valid Cases	50		

a. 1 cell (25.0%) have expected count less than 5. The minimum expected count is 1.60.
b. Computed only for a 2x2 table

Table 2 Clinical manifestations of Henöch Schonlein Purpura

Clinical Presentation	No of patients	Percentage (%)
Duration at presentation:		
Less than 1 week	24	48
>/= 1 week to < 2 weeks	7	
>/= 2 weeks to < 1 month	7	
>/= 1 month	12	
Cutaneous morphology:		
Palpable purpura	50	100
Vesico-bullous vasculitis	6	12
Vasculitic ulcer	2	4
Distribution:		
Upper limbs	28	56
Hands	7	14
Forearms and arms	25	50
Trunk	10	20
Lower Limbs	50	100
Gluteal region	21	42
Articular Syndrome	25	50
Digestive Syndrome	30	60
Digestive haemorrhage	8	16
Renal involvement	38	76
HSP post Streptococcus infection	16	32
Associated systemic Illness		
Hepatocellular Ca	1	
Metastatic mitotic lesions of unknown primary	1	
Gullain Barre Syndrome	1	
Infective endocarditis	1	
Varicella Zoster Infection	1	



Parametric correlation is used as both are categorical data

Correlation

		hand finger	haem + prot
hand finger	Pearson Correlation	1.000	.298*
	Sig. (2-tailed)		.036
	N	50.000	50
haem + prot	Pearson Correlation	.298*	1.000
	Sig. (2-tailed)	.036	
	N	50	50.000

** Correlation is significant at the 0.05 level (2-tailed)*

Discussion

Henoch Schonlein Purpura was one of the commonest causes of leucocytoclastic vasculitis (LCV) in our centre. Other common causes of LCV include drug induced, infection and connective tissue disease. There were 50 reported HSP cases in Selayang Hospital between 2003 and 2007.

The racial predilection of HSP among the ethnic Malays probably reflects the pattern of racial attendance in the clinic. However, we believe that this number was underestimated as smaller Malay communities still reside in rural areas and uncomplicated HSP especially among children were under diagnosed. The palpable purpuric rash was not the initial presenting sign in one-quarter of pediatric case and in infants; they tend to be a milder disease. Although the majority of cases were seen by dermatologist within 1 week of symptom, there were still cases seen after months of symptom onset. This could be explained by the lack of urgency by primary care doctors in referring patients with suspected with HSP to the tertiary hospital centre.

Although previous studies had showed male predominance (1.5:1)[8,9], our study showed adult HSP had an overall female predominance (1.2:1). The reason of this remains unclear. The children group however, showed male predominance.

HSP is infrequent in adults over the age of 20. A study by *Gedalia A et al*[10], showed that 75% of patients were between 2 to 11 years of age. *Blanco R et al*[3] and *Gedalia A et al* found that 50% of their study population were aged l5 years or less. Adult HSP may manifest with blisters and necrosis although this is rare in children. None of the children in our study manifested with a vasulitic ulcer. This is in contrast to a study by Blancho et al[3] where there was a significantly higher proportion of cutaneous ulcers in the adult population. Vesico-bullous vasculitis was found in 20% of the children group and 11% in adult group. It is worth mentioning that the cutaneous morphology of HSP in pediatric case has a tendency to become as severe as adult patient.

Overall, our study also showed a lower incidence of articular syndromes. Symptoms of polyarthralgias were reported to present in more than 80% of patients[1]. They most commonly affect the knees and ankles and are often associated with edema. Gastrointestinal manifestations are also common symptoms in patients with HSP; including abdominal pain in 50%-75% of subjects, melena or guaiac-positive stools in 50%, haematemesis in 30%, massive haemorrhage in 2%, and intussusception in 2%[11,12,13]. Our study showed 60% had gastrointestinal involvement and 16% gastrointestinal haemorrhage as evidence by a positive of stool occult blood and decrease in haemoglobin. None of our patients presented with massive haemorrhage. Higher percentage (20%) occurrence of digestive haemorrhage was found among children compared to 16% in the adult group. Adult HSP is characterized by a lower frequency of abdominal pain and fever, and a higher frequency of joint symptoms and renal involvement[3,4]. These findings were challenged by a study by *Blancho et al* who found that adults had a significantly higher proportion of melena. However, the gastrointestinal manifestations were noted to be more severe in the adult patients. Renal involvement was high in our study which reflected the dominant adult patients in our study. Severity of haematuria and protenuria had significant predictive factors for chronic kidney disease. The high number of adult HSP in our centre raised a concern of long term sequelae of renal complications. Proper long term medical follow-up is required.

A few studies have looked at the outcome and prognostic factors and also predictive factors of HSP associated with glomerulonephritis in adult patients[5,6,7.] However, as the researchers were mainly nephrologists, none observed the cutaneous manifestation in detail. There was a significant association and correlation between extent of rash distribution and severity of disease outcomes. This was consistent with a study by *Tancrede-Bohin E et al*[7] who showed that the spread of purpura to the trunk was one of the predictive factors of renal involvement. Our study found that there was no significant association between the severity of cutaneous morphology and severity disease outcomes. As the occurrence of these presentations is rare, a higher number of cases is probably required to contribute to statistical analysis conclusion. Lastly, the cutaneous clinical presentations didn't signify HSP trigger factor although isolated cases of HSP associated with malignancy did demonstrate the severity in extent and morphology of cutaneous presentation.

An epidemio-clinical study focusing on cutaneous presentation of HSP as one of the predictive factors of renal and gastrointestinal outcome in both adults and pediatric population is lacking in Malaysia. Hence, identification of this prognostic factor may permit the design of future prospective studies.

Conclusion

The result of our retrospective study demonstrated that the cutaneous clinical presentation is one of the predictive factors of renal and gastrointestinal outcomes in HSP. However, for more definitive conclusions, a prospective study would help in confirming the results of our study.

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Program
Incorporation of the 2nd Meeting of the AADV

AUTOIMMUNE DISORDERS - Case Report

Acute cardiac failure in a young atopic patient

Pan JY[1], MRCP, Yong WH[2], FAMS, Audrey TWH[1], FAMS

Keywords *acute cardiac failure, atopic, Churg-Strauss*

Introduction

Churg-Strauss syndrome is a granulomatous small-vessel vasculitis in which multiple organ systems can be involved. It is often diagnosed late and physicians need to be vigilant and keep this uncommon diagnosis in mind. The appearance of visible cutaneous features is often the key to diagnosis and skin biopsy is confirmatory. Early recognition and aggressive therapy is required to prevent end-organ complications and mortality.

Case report

A 21 year old Chinese female event organiser presented with a one-month history of intermittent fever with myalgia, lethargy and loose stools. Her diarrhoea had been persistent and she was admitted for intravenous rehydration for a period of two days earlier in the month. Over a period of three days, she developed bilateral lower limb swelling, a non-productive cough with shortness of breath, and scattered non-painful hemorrhagic vesicles on the lower limbs and elbows.

She was a lifelong non-smoker and had a past history of asthma since childhood for which she has had multiple admissions for exacerbations. She was on inhaled beta-agonists and inhaled corticosteroids. She had occasional short courses of oral corticosteroids during flares, but had never taken oral leukotriene antagonists before. She also had allergic rhinitis and chronic sinusitis, for which she underwent a frontal ethmoidectomy and fibreoptic endoscopic sinus surgery in November 2007.

On examination, she was afebrile but tachypnoeic at rest. She had an elevated jugular venous pressure, basal crepitations on auscultation of the lungs and bilateral pitting oedema of the lower limbs to the level of the knees. Her blood pressure and heart sounds were normal and she did not have any murmurs on auscultation. Abdominal examination revealed mild hepatomegaly but no splenomegaly and the kidneys were not ballotable. Multiple hemorrhagic vesicles and papules were noted on her feet, shins, ankles, knees and elbows (Figure 1). There was no evidence of joint swelling or synovitis.

Investigation

Investigations showed a haemoglobin value of 12.4 g/dL, a white blood cell count of 24.8 x 10^9/L (with 15.8% eosinophils) and a platelet count of 360 x 10^9/L. Urea, creatinine and electrolytes were normal. Liver function tests revealed a raised alkaline phosphatase (139U/L) and gamma-glutamyltransferase (94U/L), with hypoalbuminaemia (32g/L). Erythrocyte sedimentation rate (34 mg/L) and C-reactive protein (35.6mg/L) were both raised. Brain natriuretic peptide was raised (960 pg/mL). Creatinine kinase was normal but Troponin I was mildly elevated (0.84 ug/L). Urine microscopy showed mild haematuria and pyuria.

The chest X-ray showed bilateral basal pulmonary infiltrates and widening of the cardiac silhouette. Electrocardiography revealed small voltages compatible with a pericardial effusion. A skin biopsy of the hemorrhagic blisters showed leucocytoclastic vasculitis with eosinophils in the dermis (Figure 2), and direct immunofluorescence revealed deposits of IgM and C3 on the basement membrane. The patient was negative for anti-nuclear antibodies and anti-neutrophil cytoplasmic antibodies. She had a rheumatoid factor titre of >200 RU/ml, and hepatitis B and C serologies were negative.

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Differential diagnosis

Given the presentation of hemorrhagic vesicles and blisters, breathlessness, pulmonary infilitrates and persistent gastroenteritis, the differential diagnosis of systemic vasculitis and hypereosinophilic syndrome was considered.

In view of the long preceding history of asthma and atopy, presence of eosinophila associated with evidence of a pericardial effusion and heart failure, raised cardiac troponins, a vasculitic lower limb rash and gastrointestinal symptoms, the diagnosis of Churg-Strauss syndrome was made.

A high-resolution computerised tomography of the thorax revealed bilateral pulmonary infiltrates in the lower lobes, and cardiomegaly with a prominent pericardial effusion. Computerised tomography of the abdomen showed multiple irregular hypodense lesions in the liver, spleen and kidneys suspicious of microinfarcts from small vessel vasculitis (Figure 3). 2-dimensional echocardiography showed a reduced ejection fraction of 30%, with global hypokinesia and a moderate pericardial effusion.

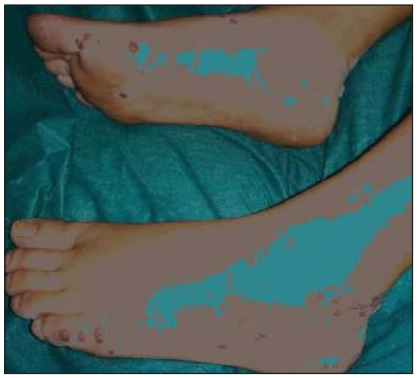

Figure 1 Hemorrhagic Blisters on the Feet

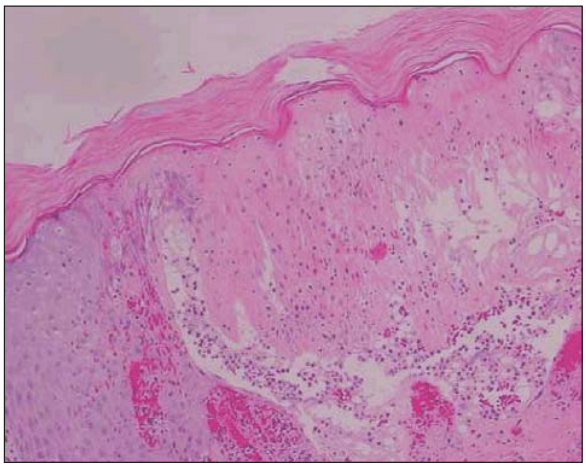

Figure 2 Leukocytoclastic Vasculitis

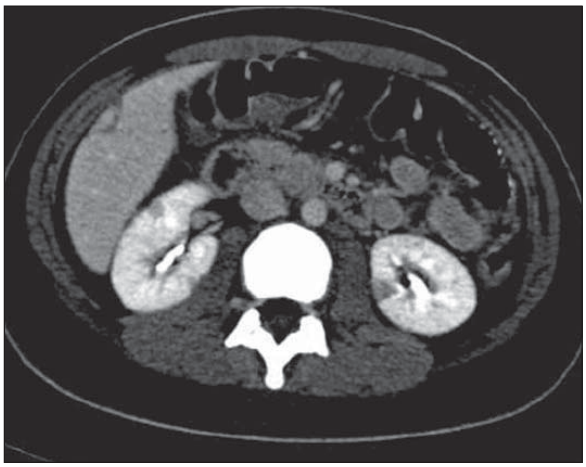

Figure 3 Vasculitic Infarcts in the Liver and Kidneys

Management and clinical course

The patient was initially treated with intravenous hydrocortisone at 100 mg 6 hourly for 2 days, followed by pulsed methylprednisolone at 500mg daily for 3 days. She was also given an intravenous infusion of cyclophosphamide at 700mg daily for 4 days.

With this treatment, the patient's symptoms recovered significantly, with improvement of lower limb swelling and resolution of the breathlessness and diarrhoea. The vasculitic lesions on her lower limbs and elbows also started to resolve. She was discharged on oral prednisolone 45 mg daily and enalapril 2.5mg twice a day. On follow-up, the cutaneous lesions were mostly healed with no scarring.

Discussion

Allergic rhinitis, asthma, and prominent blood eosinophilia are key features of Churg-Strauss syndrome[1]. It is believed to be an autoimmune process due to prominent allergic features, altered T-cell and humoral immunity, and vasculitis with circulating IgE-containing immune complexes[2]. The skin, lungs, gastrointestinal, kidneys, cardiovascular and nervous systems are often involved.

Accurate diagnosis of Churg-Strauss syndrome is difficult as individual features of the syndrome can occur in isolation, and there may be a large temporal gap before additional features appear. For example, in our patient, she had chronic relapsing asthma since childhood, together with chronic sinusitis which required surgery. As these conditions are common in our general population, the attending physician may not be alerted to this underlying condition until other symptoms occur.

In 1990, the American College of Rheumatology (ACR) developed the following criteria[3] to characterize Churg-Strauss syndrome: (1) asthma, (2) blood eosinophilia > 10% (differential leukocyte count), (3) mononeuropathy / polyneuropathy, (4) migratory lung infiltrates, (5) paranasal sinus abnormalities, and (6) histology showing a blood vessel with extravascular granulomas. The finding of 4 of the 6 criteria has a sensitivity of 85% and a specificity of 99.7% in the diagnosis of Churg-Strauss syndrome.

The clinical course occurs in 3 phases. The prodromal phase usually occurs when the patient is in his twenties or thirties, presenting with late-onset respiratory atopy: (allergic rhinitis and asthma) which is often severe. However, our patient had asthma from a very young age (3 years old) requiring multiple admissions, together with allergic rhinitis and sinusitis.

Asthma severity and the number of exacerbations may increase as the prodromal phase progresses. However, prolonged treatment of asthma may partially suppress the signs of untreated Churg-Strauss syndrome, and the disease may not be obvious until glucocorticoids are stopped, or substituted for a leukotriene receptor antagonist[4]. Leukotriene type I receptor antagonists like montelukast block production of LTC_4, LTD_4, and LTE_4 without affecting LTB_4 receptors[5]. This results in unopposed LTB_4 activity and chemoattraction for eosinophils and neutrophils[6]. This mechanism has been postulated to be important in the pathogenesis of Churg-Strauss syndrome. Our patient did not have any history of leukotriene antagonist usage, but received about three short courses of oral prednisolone every year for the treatment of asthma exacerbations.

The second or eosinophilic phase is characterized by prominent blood eosinophilia. Multiple organs including the lung and gastrointestinal tract may be infiltrated by eosinophils. The eosinophilia that was detected on the full blood count examination of our patient during her previous admissions was attributed to her history of atopy and asthma, with corticosteroid-induced reductions in eosinophil counts.

The third phase or vasculitic phase usually occurs in the mid-thirties to forties. Systemic vasculitis of the small and medium vessels may occur, leading to cutaneous, coronary and mesenteric vasculitis, lung infiltrates, pericarditis, peripheral neuropathy, and eosinophilic gastroenteritis. Our patient probably entered the vasculitic phase over a month's period, where she developed fever, breathlessness and persistent diarrhea due to eosinophilic gastroenteritis, culminating in the symptoms of cardiac failure and hemorrhagic papules and blisters on the legs over the duration of three days. The cutaneous manifestations were instrumental in alerting the attending physician to the possibility of

Churg-Strauss Syndrome and the histological findings of leucocytoclastic vasculitis were supportive of this diagnosis.

The cutaneous manifestations of Churg-Strauss syndrome are protean, ranging from erythema multiforme-like lesions, to petechiae, purpura and ecchymosis, urticarial wheals, and tender subcutaneous nodules[7]. Two-thirds of patients in the vasculitic phase of disease have cutaneous lesions. The classic histologic findings are eosinophilic granulomas surrounded by macrophages and giant cells. These granulomas are the reason for the classical description of Churg-Strauss syndrome - `allergic granulomatous angiitis'[8]. A small vessel necrotizing vasculitis may be also be commonly found Cardiovascular disease is a frequent cause of mortality in Churg-Strauss syndrome[9]. Our patient had evidence of pericarditis, pericardial effusion, myocardial injury with elevated cardiac troponins and heart failure with a reduced ejection fraction. Early corticosteroid and azathioprine therapy has been shown to halt worsening of biventricular function, leading to resolution of pericardial effusions[10]. Our patient responded well to the methylprednisolone and cyclophosphamide regime described above.

Allergic rhinitis is extremely common[8]. Other forms of nasal and sinus involvement include recurrent sinusitis and nasal polyposis. Exophthalmos, deafmess, chronic otitis, and eosinophilic granulomatous infiltration of the skull base are rare late complications. Necrotizing lesions of the nasopharynx and upper airway are uncommon compared to Wegener Granulomatosis[11].

Peripheral neuropathy or mononeuritis multiplex may occur in up to 75% of patients[12], which may worsen to involve multiple nerves if untreated[13]. Cerebral hemorrhage and infarction are important causes of death. Joint and muscle involvement are rare.

About 27% of patients have kidney involvement[14]. Disease severity ranges from proteinuria and microscopic hematuria to renal insufficiency. However, renal failure is uncommon and occurs in less than 10% of patients, unlike Wegener's granulomatosis[15]. Renal infarction may result in secondary hypertension. Our patient had mild hematuria on urine microscopy, but blood pressure was normal.

An eosinophilic gastroenteritis may occur, presenting with abdominal pain, diarrhoea, or gastrointestinal bleeding. This may precede the vasculitic phase of Churg-Strauss syndrome. Our patient had diarrhoea of a month's duration preceding the onset of the vasculitic rash and was initially thought to have an infective gastroenteritis.

Systemic corticosteroids are the cornerstone of therapy, usually at high doses of 0.5-1.5 mg/kg/day for 6-12 weeks. Higher doses are needed for patients with neuropathy, cardiac or renal impairment. Eosinophil count and erythrocyte sedimentation rate can be used to monitor response to treatment and to detect relapses. Late relapses after a successful response to treatment are rare.

Cyclophosphamide, azathioprine and high dose intravenous immune globulin are useful in severe disease, including fulminant glomerulonephritis not responding to corticosteroids[16]. Glucocorticoids combined with interferon-alpha have been reported to be beneficial[17]. Plasma exchange has not been demonstrated to be useful[18]. Anti-IgE (omalizumab) was reported to improve lung function and decrease absolute eosinophil counts in a single patient[19], but more studies are required.

Most deaths occur in the vasculitic phase of the disease, and are most often due to heart failure or myocardial infarction, cerebral bleeding, kidney failure, gastrointestinal bleeding or status asthmaticus. The presence of significant cardiac or gastrointestinal disease is the strongest indicator of poor prognosis[20], and both are present in our patient.

Conclusion

Churg-Strauss syndrome is a multisystem disorder in which the diagnosis is easily missed in the early stages. Dermatologists should consider this diagnosis in atopic patients with unexplained persistent eosinophilia who develop features of cutaneous vasculitis and other systemic symptoms. Cutaneous manifestations of Churg-Strauss syndrome, in combination with other symptoms of the disease, were crucial in alerting the attending physician to this important diagnosis. Our patient has some indicators of poor prognosis and should be followed up closely to monitor for relapses.

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ANNOUNCEMENT - Administrative Update

Pain as a 5th vital sign

Mary SC, MMed (anaes)

Ministry of Health Malaysia has introduced pain as a 5th vital sign this year. It is particularly relevant in Toxic Epidermal Necrolysis where uncontrolled pain may have severe systemic consequences and increases morbidity and mortality.

Regular analgesia may be required for severe pain, given 1/2 hr prior to dressing. DF118, Tramadol morphine may be considered.

Self-administered analgesia i.e. PCA (patient controlled analgesia) with morphine may be indicated if patient is in severe pain.

After administering analgesia, we need to re-assess the patient. Increasing the dose of analgesia or changing to other analgesic may be required if the patient continues to have severe pain. Assess pain score on admission to assess the severity of pain (baseline score), 1/2 an hour after analgesics given to assess analgesic action and every time vital signs taken (4 hourly) as the 5th vital sign.

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