Clinical features and prognostic factors of cutaneous vasculitis among dermatology patients in Johor Bahru, Malaysia

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ABSTRACT

Background: Cutaneous vasculitis is common, yet the risk factors for its chronicity have not been established.

Objective: To describe the clinical spectrum and identify risk factors for chronicity of cutaneous vasculitis.

Methods: Retrospective data analysis of 275 patients diagnosed with cutaneous vasculitis from January 2008 to December 2013.

Results: The mean age was 33.7 (±17.89) years, with female predominance. The majority of patients were Malays (67.3%). Skin biopsy was performed in 110 (40%) patients. The commonest sign was palpable purpura (30.6%). The aetiology remained elusive in 51.3% of patients. Common identifiable causes include infection (19.7%) and connective tissue disease (10.2%). Extracutaneous features were noted in 46.5% of patients. Erythrocyte sedimentation rate and antinuclear antibody were raised in 124 of 170 and 27 of 175 patients with documented results respectively. Cutaneous vasculitis was the presenting symptom in seven patients with newly diagnosed systemic lupus erythematosus. Anti Streptolysin O Titre was positive in 82 of 156 patients with documented results. Despite antibiotics, 31.7% of them had chronic lesions. Prednisolone alone was used in 20% of patients while 16.4% needed steroid-sparing agents. Most patients who needed systemic therapy (62%) had unidentifiable aetiology. Among the 155 patients who remained under follow up, 36.4% had chronic disease, one patient succumbed due to septicaemia, and the rest fully recovered within three months. The presence of ulcerative lesion was significantly associated with developing chronic vasculitis (p=0.003).

Conclusion: The clinical spectrum of cutaneous vasculitis in our population was similar to other studies. Ulcerative lesion predicts a chronic outcome.

KEY WORDS:
Cutaneous vasculitis, ulcerative lesion, prognosis

INTRODUCTION

Vasculitis is defined as an inflammatory process of vessel wall, leading to its damage and subsequent haemorrhagic process.[1] It can be a primary disorder, or secondary to drugs, infections or systemic conditions such as connective tissue disease and malignancy.[2] Cutaneous involvement is a very common presentation of vasculitis.[3] Characteristic signs include palpable purpura, urticaria, infiltrated erythema, ulcer, infarct, livedo reticularis, nodules and gangrene.[4] These lesions can be accompanied by fever, joint pain or fatigue.[5] Mainstay of treatment for vasculitis is elimination of the underlying cause.[4] Systemic therapy is indicated for severe disease or with systemic involvement.[3]

The natural course of cutaneous vasculitis is unpredictable.[5] Risk factors for chronicity and severity of the disease have not been clearly identified.[5,6] To date, there are only few published data regarding cutaneous vasculitis in Malaysia.

This study aims to examine the clinical features of patients with cutaneous vasculitis, and to identify the risk factors associated with chronicity of the disease.

MATERIALS AND METHODS

The medical records of patients diagnosed clinically (based on ICD 10 coding L95) and/or histologically with cutaneous vasculitis from January 2008 to December 2013 at the Dermatology Department, Sultanah Aminah Hospital Johor Bahru, Malaysia, were analysed. Cases registered under vasculitis were selected using the clinic computer database and the case notes were screened manually. Data extracted from case notes include patient demography, clinical presentation of vasculitis, presence of systemic symptoms, possible etiological factors, history of drug intake, co-existing medical conditions, laboratory results, treatment received and disease outcome.

Classification system for vasculitis was based primarily on the definitions proposed by the Chapel Hill Consensus Conference (CHCC) 2012. Fever was defined as a temperature >37.7°C, while joint involvement included arthralgias and/or arthritis. Extracutaneous involvement was based on clinical, biochemistry or radiological findings. Renal involvement was defined as presence of persistent glomerular haematuria and/or proteinuria and/or raised serum creatinine above baseline. Gastrointestinal manifestations included bowel angina (diffuse abdominal pain worse after meals) and gastrointestinal bleeding (melaena, hematochezia, or positive stool occult blood).

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Table I: Aetiology of Cutaneous Vasculitis (n=275)

Aetiology	Number of cases (Percentage)
Idiopathic	141 (51.3%)
Septic vasculitis	34 (12.4%)
Connective tissue disease	28 (10.2%)
Streptococcal infection	20 (7.3%)
Drugs	10 (3.6%)
Henoch-Schonlein purpura	2 (0.7%)
Polyarteritis nodosa	2 (0.7%)
Malignancy	2 (0.7%)
Undetermined	36 (13.1%)

Table II: Investigation Results

Investigation	Number of patients tested	Number with bnormal results (Percentage)	Number with normal results (Percentage)
White cell count	216	58 (26.9%)	158 (73.1%)
Haemoglobin	212	49 (23.1%)	163 (76.9%)
Creatinine	186	44 (23.7%)	142 (76.3%)
Antinuclear antibody (ANA)	185	37 (20.0%)	148 (80.0%)
C-reactive protein (CRP)	175	86 (49.1%)	89 (50.9%)
Erythrocyte sedimentation rate (ESR)	170	124 (72.9%)	46 (27.1%)
Alanine transaminase (ALT)	163	24 (14.9%)	139 (85.1%)
Anti Streptolysin O Titre (ASOT)	156	82 (52.1%)	74 (47.9%)
Hepatitis B surface antigen (HBsAg)	131	1 (0.8%)	130 (99.2%)
Antibodies to Hepatitis C Virus (Anti HCV)	150	2 (1.3%)	148 (98.7%)
Antineutrophil cytoplasmic antibodies (p & c ANCA)	123	6 (4.9%)	117 (95.1%)

Table III: Therapy and Outcome (n=275)

	Number of cases (Percentage)
Therapy	
Supportive	175 (63.6%)
Oral corticosteroids	55 (20.0%)
Dapsone	35 (12.8%)
Azathioprine	7 (2.5%)
Cyclosporin	2 (0.7%)
Mycophenolate mofetil	1 (0.4%)
Outcome	
Lost to follow up	120 (43.6%)
Acute course*	98 (35.6%)
Chronic course+	56 (20.4%)
Death	1 (0.4%)

*single episode of less than 3 months' duration
+prolonged course of over 3 months or at least two recurrent episodes over a period exceeding 3 months

Histological criteria included presence of fibrinoid necrosis of vessels, neutrophilic infiltration of vessel walls, perivascular neutrophils, leukocytoclasis, red blood cell extravasation and fibrin thrombus.

The clinical course was divided into acute (single episode of less than 3 months duration) or chronic (prolonged course of over three months or at least two recurrent episodes over a period exceeding three months). In situations where both acute and chronic factors exist, the acute factor was considered as the most likely cause.

The erythrocyte sedimentation rate (ESR) was arbitrarily considered abnormal if >15mm/1 hour for males and >20mm/1 hour for females. The C-reactive protein (CRP) was considered elevated if >10mg/dL. Antinuclear antibody (ANA) and Anti Streptolysin O Titre (ASOT) were considered positive if titres were ≥1:80, and ≥200IU respectively.

Descriptive method was used for analysis of demographic data, etiologic factors and laboratory profile of patients. Patients with a known outcome (acute / chronic) were selected for comparative analysis. The chi square test and logistic regression methods were used to determine the risk factors for chronicity of the disease. $P<0.05$ was considered significant.

This study has been registered with the Malaysian National Medical Research Register (NMRR-14-639-21483) and approved by Medical Research Ethics Committee Malaysia (Research ID 21483).

Table IV: Risk Factors Associated with Chronic / Recurrent Cutaneous Vasculitis*

Risk factors	Acute course (%)	Chronic course (%)	Univariate analysis			Multivariate analysis+ p value
			Crude OR	95% CI	p value	
Age (years)						
<20	30 (81.1)	7 (18.9)	1	-	-	-
20-39	37 (56.1)	29 (43.9)	0.39	0.05-2.92	0.361	-
40-59	24 (63.2)	14 (36.8)	1.41	0.24-8.33	0.702	-
≥60	7 (50.0)	7 (50.0)	0.45	0.06-3.25	0.425	-
Ulcer						
Absent	96 (69.6)	42 (30.4)	1	-	-	-
Present	2 (11.8)	15 (88.2)	23.92	2.61-21.95	0.005	0.003
Fever						
Absent	71 (58.7)	50 (41.3)	1	-	-	-
Present	27 (79.4)	7 (20.6)	0.39	0.10-1.54	0.180	-
ANA						
Negative	58 (65.9)	30 (34.1)	1	-	-	-
Positive	6 (37.5)	10 (62.5)	3.77	1.02-13.99	0.047	0.057

* Examined using multiple logistic regression; OR: odds ratio; CI: confidence interval
\+ Forward Stepwise Likelihood Ratio was applied for multivariate analysis for significant variables in the univariate analysis. There were no interactions amongst independent variables.

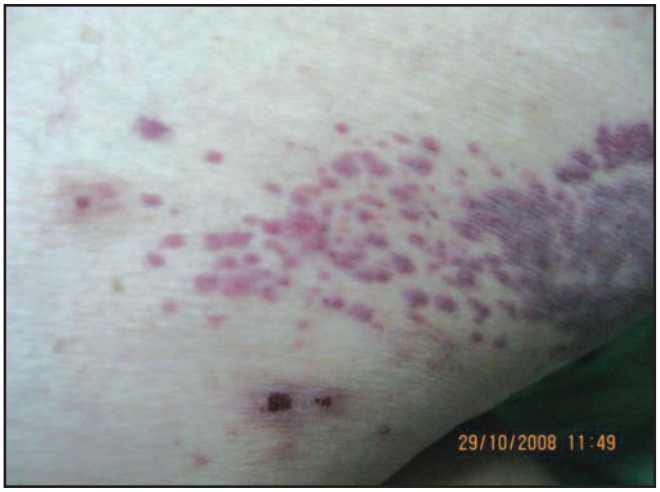

Fig. 1: Palpable purpura.

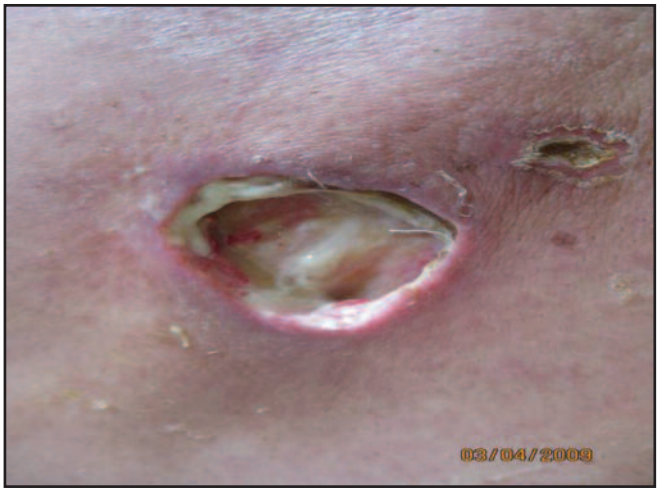

Fig. 2: Ulcerative lesions.

RESULTS

A total of 275 patients were included in this study. Females outnumbered males in a ratio of approximately 2:1 (182 females versus 93 males). The mean age was 33.7 years (range 3 months to 83 years). Patients in the age group 20 to 39 years were most frequently affected (42.2%). The racial composition was 67.3% Malays, 19.6% Chinese, 4.4% Indians and 8.7% other ethnicities. Skin biopsy was performed in 110 (40%) patients, and the commonest histopathological finding was leucocytoclastic vasculitis (72.5%).

The commonest skin lesion seen was palpable purpura (Fig 1) at 30.6%, followed by non-palpable purpura at 15.6% and ulcerative lesion (Fig 2) comprising 10.5% of patients. Extracutaneous involvement was seen in 128 (46.5%) patients, mainly fever (51.6%), arthritis/arthralgia (35.9%), renal manifestations (30.5%) and GI symptoms (5.8%). Out of 66 patients with fever, only 36 cases (54.5%) were attributed to an infectious cause.

In the majority of cases (51.3%), no etiological factor could be identified. The most frequently implicated causes include septic vasculitis (12.4%) and connective tissue disease (10.2%), as displayed in Table I. Drug-induced cause was seen in only 10 patients, with the commonest culprit drug being traditional medication (66.7%).

Investigations that were carried out and their results are summarized in Table II. Most of the investigation results were within normal range, except for raised ESR in 72.9% of 170 patients with documented ESR. No significant association was found between a raised ESR with the outcome of vasculitis. ANA titre was positive in 27 of 175 patients with available results. Cutaneous vasculitis was one of the initial presenting symptoms for seven of these patients who were subsequently diagnosed with systemic lupus erythematosus (SLE). ASOT was positive in 82 of 156 patients with documented results. Among the 82, 31.7% showed chronic progression despite a complete course of antibiotics. These patients had ASOT readings between 200 to 800 IU. Antineutrophil cytoplasmic antibodies (ANCA) were positive only in 4.9% of patients who had the test done.

Systemic immunosuppressive therapy was used in 36.4% of patients (Table III). Oral prednisolone was usually prescribed at a dose of 0.5 to 1mg/kg for patients with persistent or recurrent lesions, or with significant extracutaneous symptoms. Dapsone was the commonest first line steroid sparing agent used. The majority who needed systemic immunosuppressive therapy had unidentified aetiology (62%).

Complete remission was seen in 63.2% of the 155 patients who remained under follow up. There was 1 death due to septicaemia (Table III).

Table IV lists the risk factors associated with chronicity of vasculitis. Further multivariate analysis showed that the presence of ulcerative lesion was the only independent risk factor for developing chronic disease (p=0.003).

DISCUSSION

To date, they are very few published data on the clinical spectrum of cutaneous vasculitis in Malaysia. The risk factors associated with chronicity of the disease have also not been established.

The clinical spectrum of cutaneous vasculitis in our study was similar to most other previous studies.[6-12] The commonest age group affected was between 20 and 39 years, with a female preponderance. Palpable purpura was the most prevalent lesion, likely so as it has been found to be a sensitive diagnostic sign of cutaneous vasculitis.[11] Extracutaneous manifestations were common, mainly involving the kidneys, gastrointestinal tract and joints, similar to other studies.[6,7]

The aetiology of cutaneous vasculitis was not identifiable in the majority of our patients, similar to previous studies.[6-12] However, contrary to previous studies,[6-10] we found a low incidence of a drug-induced cause in our study. This finding may be attributed to a possible recall bias of drug intake by the patients.

Most investigation results were within normal range, except for a raised ESR seen in more than two thirds of our cases. However, a raised ESR is non-specific and cannot be used as a guide for treatment or management of cutaneous vasculitis. The ANCAs are expensive tests and were found to be positive only in a very small number of patients. Previous studies done also similarly found that most laboratory tests performed were within normal range.[6-9] These findings question the usefulness and cost-effectiveness in performing multiple investigations for all patients with vasculitis. A good approach would be to perform only pertinent investigations for isolated vasculitis with no systemic involvement, while more extensive tests should be reserved for chronic or recurrent vasculitis with unknown aetiology.[13]

Positive ANA titres were seen in 15.4% of cases with available results. About a quarter (25.9%) of these cases were newly diagnosed with SLE with cutaneous vasculitis as part of the presenting symptom. Therefore, a positive ANA titre in the setting of a patient with cutaneous vasculitis warrants further evaluation for an underlying connective tissue disorder, especially if accompanied by chronic or recurrent lesions.
Almost one third of our patients with a positive ASOT titre did not recover after completion of antibiotics. A raised ASOT titre with cutaneous vasculitis is often taken as a presumptive diagnosis of a recent streptococcal infection, and a course of antibiotics is usually prescribed. However, persistence or recurrence of lesions despite treatment may indicate an alternative cause, and warrant repeated investigations and long term follow up.[14]

Systemic therapy for cutaneous vasculitis is often deferred as most cases resolve with only bed rest and analgesia.[1,2,13,14] However, some cases may require systemic therapy to hasten recovery and reduce morbidity. Identifying the prognostic factors will therefore be helpful in deciding for early initiation of systemic therapy. In previous studies, older age (>40 years), raised ESR, absence of fever and presence of arthralgia have been identified as poor prognostic factors for cutaneous vasculitis.[5,6] Our study showed that the presence of ulcerative lesion and a positive ANA titre were significantly associated with poorer prognosis on univariate analysis. However, multivariate analysis showed that the presence of ulcerative lesion was the only significant poor prognostic factor for cutaneous vasculitis. This finding could suggest for early initiation of systemic therapy in patients with vasculitis who present with ulcerative lesions.

Our limitations include the fact that this was a retrospective study, and not all cases were confirmed histologically.

CONCLUSION

The clinical spectrum of cutaneous vasculitis in our population was similar to other studies done worldwide. The identified prognostic factors can aid the clinician in managing these patients.

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