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Cutaneous Vasculitis Seen at a Skin Referral Centre in Singapore

S H Chua, J T E Lim, C B Ang

ABSTRACT

Objective: To study the clinical features and course of patients presenting to a skin referral centre with cutaneous vasculitis.

Method: A retrospective review of patients presenting to the National Skin Centre from 1993 to 1995 with cutaneous vasculitis was done. All patients included in the study had histologically proven vasculitis on skin biopsy. The clinical manifestations and laboratory investigations of the patients were recorded. The response to the various drugs given as first line therapy and course of the disease 1 year after initial presentation was reviewed.

Results: Forty- seven patients were included in this study. Females outnumbered males in a ratio of approximately 2:1 (32 females versus 15 males). The age of the patients ranged from 14 to 78 years, with a mean of 36 years. The aetiology remained elusive in 70% of cases. Of the known secondary causes, drugs and streptococcal infections were the most frequently implicated. The lower limbs were involved in more than 90% of cases. Cutaneous lesions took the form of palpable purpura, ulcers, nodules and urticaria. Extracutaneous manifestations were present in 47% of patients. The main extracutaneous manifestations were arthralgia/arthritis (21%), microscopic haematuria (16%) and abdominal pain (8%). Direct immunoflourescence on lesional skin was positive in 65% of cases. A raised erythrocyte sedimentation rate was observed in 40% of patients. Positive anti-nuclear antibodies were detected in 30% of cases. Most patients who were given systemic corticosteriods responded predictably well. The response to other modalities of treatment was more variable. At 1 year follow-up, complete remission was recorded in 47% of the patients, while in 53% of the patients, the disease continued to run a chronic relapsing course.

Keywords: leukocytoclasis, palpable purpura, urticarial vasculitis, vasculitic ulcers, direct immunoflourescence

National Skin Centre
1 Mandalay Road
Singapore 308205

S H Chua, FAMS, MBBS, MRCP (UK)
Registrar

J T E Lim, FAMS, MBBS, FRCP (Ire)
Consultant

820 Thomson Road
#01-05
Mt Alvernia Medical Centre
Singapore 574623

C B Ang, FAMS, MBBS, MRCP (UK)
Consultant Dermatologist

Correspondence to:
Dr S H Chua

INTRODUCTION

Cutaneous vasculitis presents in a variety of morphological lesions that may be self-limiting or relapsing. The vasculitis may be idiopathic or an underlying cause such as drugs, streptococcal infection or connective tissue disease may be present. Cutaneous lesions may be the sole manifestation of the vasculitis or may be part of a more extensive involvement affecting other organs. In this retrospective review, we examined the clinical features and laboratory abnormalities of patients presenting to the National Skin Centre with histologically proven cutaneous vasculitis.

MATERIALS AND METHODS

A retrospective review of patients presenting to the National Skin Centre from 1993 to 1995 with cutaneous vasculitis was done. All patients included in the study had histologically proven vasculitis on skin biopsy. Histological evidence of vasculitis included the presence of either endothelial swelling, fibrinoid necrosis of the blood vessel walls, perivascular dermal haemorrhage or leukocytoclasis. An attempt to identify the aetiology from either history or by investigations was carried out. Patients were screened for any associated systemic complications. A combination of investigations carried out included direct immunoflourescence (DIF) on lesional skin, anti-streptococcal O lysin titre (ASOT), hepatitis B surface antigen assay (HBsAg), anti-nuclear antibody assay (ANA), rheumatoid factor (RF), full blood counts, erythrocyte sedimentation rate (ESR), serum electrolytes, liver function tests (LFT), serum complements, serum cryoglobulins, and chest radiographs. These tests were performed on some but not all of the patients in the study population. The response to the various drugs given as first line therapy was recorded. The course of the disease 1 year after initial presentation was reviewed.

RESULTS

A total of 47 patients were included in the study. Females outnumbered males in a ratio of approximately 2:1 (32 females versus 15 males). The age of the patients ranged from 14 to 78 years, with a mean of 36 years. The racial composition was 38 Chinese, 2 Malays and 7 Indians. The average duration between onset of symptoms and diagnosis was 21 days, with most patients either self-medicating or seeking treatment from primary level physicians before presentation to the National Skin Centre.

The aetiology of cutaneous vasculitis is summarised in Table I. In the majority of cases, no

Table I – Aetiology of cutaneous vasculitis

Aetiology	No. of patients (%)	
Idiopathic	34	(72.4%)
Drugs	4	(8.5%)
Streptococcal infection	3	(6.4%)
Systemic lupus erythematosus	2	(4.3%)
Cutaneous polyarthritis	1	(2.1%)
Inflammatory bowel disease	1	(2.1%)
Cryoglobulinaemia	1	(2.1%)
Seronegative arthritis	1	(2.1%)

cause was found, but of the known secondary causes, drugs and streptococcal infections were the most frequently implicated. The sites of involvement were lower limbs only (68%), lower limbs and upper limbs (13%) and generalised (21%). The primary lesions were palpable purpura in 16 patients (Fig 1), ulcers in 11 patients (Fig 2), nodules in 5 patients (Fig 3) and urticarial plaques in 4 patients (Fig 4). The remaining 13 patients had a combination of the above lesions. Bacterial cultures from the ulcers grew *Staphylococcus aureus* (5/11), *Pseudomonas species* (2/11), *Escherichia coli* (1/11) and mixed bacterial growth (1/11). No bacterial growth was reported in the remaining 2 cases.

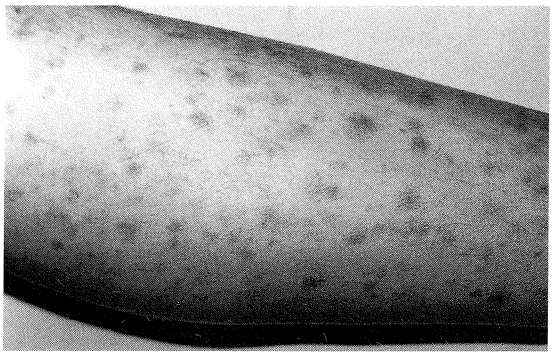

Fig 1 – Palpable purpura in cutaneous vasculitis.

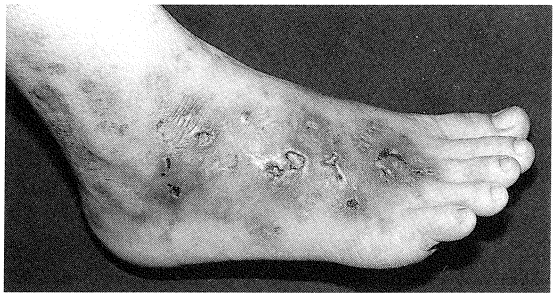

Fig 2 – Ulcerative lesions in cutaneous vasculitis.

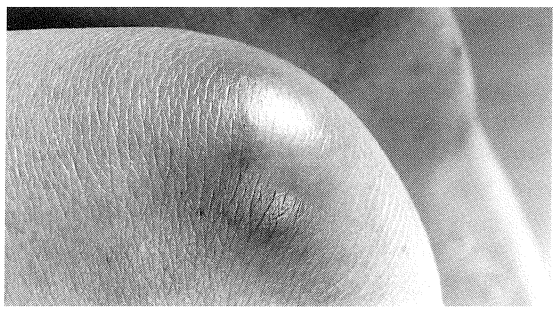

Fig 3 – Nodular lesions in cutaneous vasculitis.

Extracutaneous manifestations were present in 48% of patients (18/38). The main extracutaneous manifestations were arthralgia/arthritis (8/38), microscopic haematuria (6/38), abdominal pain (3/38) and fever with chills (1/38). Direct immunoflourescence (DIF) on lesional skin was performed in 34 patients. Positive DIF findings were reported in 65% (22/34) of cases. The frequency of deposition of the various immunoreactants in patients with positive DIF findings is summarised in Table II.

The results of the basic haematological and biochemical investigations performed were haemoglobin 8.6 – 16.6 g/dL (normal range: 12 – 18 g/dL), leucocytes 3,600 – 16,400/mm^3 (normal range: 4,000 – 10,000/mm^3), platelets 150 – 400 x $10^3/mm^3$ (normal range: 140 – 440 x $10^3/mm^3$), urea 2.4 – 7.1 mmol/L (normal range: 3.3.2 – 7.1 mmol/L, creatinine 47 – 125 μmol/L (normal range: 71 – 133 μmol/L), total protein 64 – 88 g/L (normal range: 63 – 82 g/L), albumin 36 – 52 g/L (normal range: 39 – 50 g/L), and alanine transaminase 5 – 55 U/L (normal range: 13 – 61 U/L. The results of the rest of the investigations performed are summarised in Table III. A raised ESR was observed in 40% of patients; but this did not correlate with the severity of the cutaneous vasculitis seen. Positive anti-nuclear antibodies were detected in 30% of cases. In terms of therapy, the first line therapy given were oral prednisolone (n = 22), colchicine (n = 13), dapsone (n = 5), others (n = 6) and no treatment (n = 1); others included topical corticosteriods, antihistamines and indomethacin. The choice of first line therapy was largely empirical. Oral prednisolone at a starting dose of 0.5 to 1 mg/kg was most frequently prescribed for patients presenting with severe ulcero-necrotic lesions or for patients with significant extra-cutaneous symptoms. These patients were often reviewed weekly and the dose of prednisolone adjusted according to clinical response. Patients with less severe clinical manifestations eg. those presenting with palpable purpura were often started on alternative therapy of which oral colchicine at a dose of 0.5 mg taken twice or three times daily was most frequently prescribed. The response to the various treatments is summarised in Table IV. Most patients showed predictably good response to oral prednisolone. Response to the other modalities of treatment was more variable and inconsistent. One year follow-up records were available for 34 patients. Complete remission was recorded in 47% of the patients (16/18), while in 53% of the patients, the disease ran a chronic relapsing course.

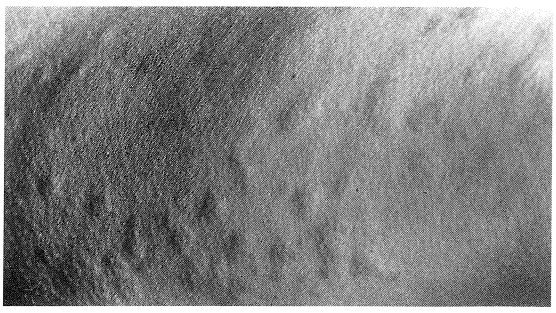

Fig 4 – Urticarial lesions in cutaneous vasculitis.

Table II – Types of immunoreactants deposited in the walls of blood vessels of patients with positive immunoflourescence findings

Immunoreactant	No. of patients
C3	16
Fibrinogen	14
C1q	10
IgM	2
IgG	2
IgA	2

In patients with positive direct immunoflourescence findings, the immunoreactants are deposited singly or in combination. This table reflects the cumulative total of all immunodeposits observed.

Table III – Other investigation results

Investigation	Number of patients tested	Abnormal	Normal
ESR	31	9 raised (> 20 mm/hr)	22
ANA	28	9 positives	19 negatives
Rheumatoid factor	19	0 positive	19 negatives
ASOT	17	3 raised titres	14
HBs Ag	15	0 positive	15 negatives
Complement levels	12	1 low	11
Cryoglobulins	15	1 positive	14 negatives

ESR = erythrocyte sedimentation rate
ANA = anti-nuclear antibody
ASOT = anti-streptococcal O lysin titre
Hbs Ag = hepatitis B surface antigen

Table IV – First line treatment given to patients and the response rate

First line treatment	No. of patients	Response rate
Prenisolone	22	90%
Colchicine	13	69%
Dapsone	5	40%
Topical steroids	3	33%
Indomethacin	1	-
Antihistamines	1	-
Erythromycin	1	-
No treatment	1	-

DISCUSSION

Cutaneous vasculitis may present in a variety of clinical lesions, the most common of which is palpable purpura. Ulcers are less common but tend to cause more discomfort and morbidity. Superimposed bacterial infections of the vasculitic ulcers are common and can cause delayed healing of the vasculitic ulcers unless they are diagnosed early by wound cultures and treated with appropriate antimicrobials. The most common pathogen found in this study was *Staptylococcus aureus* which is responsive to systemic cloxacillin. The lower limbs are preferentially affected, and this is likely to be related to the effect of gravitational vascular stasis. The distribution of lesions, however, has no bearing to the etiology or sex distribution. The diagnosis of cutaneous vasculitis may be slightly delayed as patients tended to self-medicate in the initial phases of their disease or the condition may be misdiagnosed by primary level physicians who are unfamiliar with the presentation of cutaneous vasculitis. In our study, young adult females appeared to be primarily affected although children and the elderly may be affected as well.

The aetiology of cutaneous vasculitis remains elusive in 70% of cases. Of the known secondary causes, drugs and streptococcal infections were the most frequently implicated. In 2 patients, the cutaneous lesions were the presenting symptoms of an underlying systemic vasculitis – systemic lupus erythematosus. An acute precipitating cause such as drugs or infection is related to a better prognosis as the cutaneous vasculitis may resolve when the precipitating cause is removed. On the other hand, an underlying chronic illness such as collagen vascular disease is related to a less favourable outcome. It has been suggested that the presentation of palpable purpura is associated with a better prognosis compared with the presentation of vasculitic ulcers[1].

Routine histology is the most important diagnostic investigation required, and cutaneous vasculitis can only be diagnosed if histological evidence of endothelial swelling, leukocytoclasis, fibrinoid necrosis of blood vessel walls or extravasation of red blood cells is seen[2]. The inflammatory infiltrate seen on histology is dynamic, with neutrophils predominating in the early lesions and monocytes predominating in late lesions[3]. Direct immunoflourescence of lesional skin is a useful additional diagnostic tool but may be negative in 20% to 40% of cases and is therefore not essential for the diagnosis of cutaneous vasculitis[4]. The concomitant presence of immune deposits along the dermo-epidermal junction may however suggest lupus erythematosus as an underlying cause[2].

A slightly raised ESR is observed in 40% of patients. This finding is non-specific and cannot be used as a guide for treatment or prognosis. Hypocomplementaemia was detected in 1 patient who had systemic lupus erythematosus. Complement reduction may indicate more aggressive vascular involvement and a poorer prognosis[5]. Positive anti-nuclear antibodies can be detected in 30% of cases. Low titres appear to be non-specific but evaluation for an underlying collagen vascular disorder is nevertheless required in all positive cases. High titres of ANA require close monitoring over a period of time to exclude evolvement into a systemic vasculitis. A raised ASOT is often taken as a presumptive diagnosis of recent streptococcal infection and a course of anti-streptococcal antimicrobial therapy may be given in an attempt to eliminate the source of infection and hasten the resolution of the cutaneous vasculitis.

In addition to the removal of triggers and supportive nursing care, treatment of acute severe episodes of cutaneous vasculitis may require a short course of systemic corticosteriods to minimise morbidity. Although systemic corticosteriods are effective in most cases[6], alternative therapy with less side-effects should be considered in less severe cases. The choice of alternative therapy is often empirical as controlled efficacy trials using colchicine[7,8], dapsone[9,10], antihistamines and non-steroidal anti-inflammatory agents[11] in the treatment of cutaneous vasculitis are unfortunately lacking. Based on the results of this study, we recommend that short-term systemic prednisolone at a starting dose of 0.5 to 1 mg/kg be considered as first line therapy in patients with severe ulcero-necrotic vasculitic lesions and in patients with systemic vasculitis. The dose of prednisolone can be gradually tapered down and taken off as the patient improves clinically. In patients with non ulcero-necrotic lesions eg. palpable purpura, colchicine 0.5 mg taken twice daily or three times daily can be used as first line therapy instead. The concern of dapsone hypersensitivity syndrome often limits the use of dapsone as a first line therapy in cutaneous vasculitis. Potent topical steriods may be useful as an adjunctive topical treatment together with any systemic therapy employed.

The prognosis of cutaneous vasculitis is dependent on whether an antigenic source can be identified and eliminated. In 50% of cases, the disease may run a chronic relapsing cause although severe systemic involvement remains uncommon.

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