Practical Approach to Vasculitis*

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INTRODUCTION

Vasculitis is one of the diagnoses frequently considered during the examination of a patient with multisystem disease of uncertain nature. Its manifestations are protean thus making diagnosis sometimes difficult and all encompassing. This paper is aimed at minimizing the confusion and enabling a physician to diagnose and treat vasculitis with confidence and efficacy. However, it is not intended to be an extensive review of vasculitis; readers who want more depth are referred to several recent reviews.[1-6] The main view-points in this paper are drawn from the experience gained at the University of Colorado's Allergic Disease Center (Vasculitis Study Group) and later from treating patients in Thailand.

Approaching a patient with vasculitis

Table 1 lists the essential steps to be taken when encountering a possible case of vasculitis. These steps should be carried out sequentially

Table 1. Approaches to a patient with vasculitis.

1. **Clinical recognition** that vasculitis exists. This is determined by:
   i) *Well-defined clinical syndromes,* e.g. Henoch-Schonlein purpura, allergic granulomatosis, Wegener's granulomatosis, giant cell arteritis, Takayasu's arteritis and mucocutaneous lymph node syndrome.
   ii) *Pathognomonic signs*
      a) Palpable purpura
      b) Retinal vasculitis
   iii) *Multisystem disease* including fever of unknown origin and unexplained weight loss
2. **Identify and confirm the type of vasculitis that the patient has by:**
   i) Histopathology – vessel size, cellular infiltrate, granulomata and necrosis (however, overlapse may occur.)
   ii) Immunopathology
   iii) Radiography – chest, sinus, artery (fluorescein, renal, mesenteric, aortic)
3. **Supportive laboratory evidences for vasculitis** – Complete blood count, Urinalysis, ESR, complement, cryoglobulins, circulating immune complexes, etc.
4. **Identify and remove the aetiologic agent (if found),** e.g. drug, infection, connective tissue diseases.
5. **Clinical staging** – which organ has been involved?
   – For therapeutic and prognostic values
   – For follow-up
6. **Institute a regimen of drug** (s) the efficacy of which has been proven for that particular form of vasculitis at that clinical stage.
7. **Follow the patient's progress;** taper off or discontinue the drug. At the same time, prevent relapse or progression of the vasculitis process.

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in order to arrive at a sound diagnosis and method of treatment.

I. Clinical recognition of vasculitis

1. Well-defined clinicalsyndromes

Certain vasculitides have pathognomonic signs and symptoms. Thus, by memorizing the syndromes, a physician may be able to recognize the disease early and provide suitable treatment. For example, Henoch-Schönlein purpura is characterized in youngsters by palpable purpura, arthralgia, haematuria and abdominal pain, usually following an upper respiratory tract infection.[5] Allergic granulomatosis of Churg and Strauss is typified by intractable asthma, peripheral eosinophilia, fever, lung infiltration and at times, skin nodules and papules.[7] Characteristic features of Wegener's granulomatosis are granulomatous involvements of upper and lower airways together with glomerulonephritis.[8] Giant cell arteritis is a disease of the elderly featuring unilateral throbbing headache over the temporal areas, jaw claudication, high erythrocyte sedimentation rate and sudden blindness.[9] Takayasu's arteritis is a disease found in young Oriental adults with hypertension and unilateral absence of peripheral pulses (pulseless disease).[10] Mucocutaneous lymph node syndrome (Kawasaki disease) is a disease, mainly of Oriental children, characterized by fever, cervical lymphadenopathy and characteristic mucocutaneous lesions as well as coronary artery involvement.[11]

2. Pathognomonic signs

Palpable purpura (Figure 1) is the pathognomonic sign of cutaneous venulitis. It is typically different from flat thrombocytopenic purpura. Retinal vasculitis is another entity among vasculitides; it is easily recognized by an experienced ophthalmologist, often even when pathological proof is lacking. It is characterized by engorgement and irregularity of retinal vessels, perivascular sheathing, retinal haemorrhages and neovascularization in late phases. In addition, angiographic demonstration of multiple microaneurysms at the endarteries is also diagnostic for the arterial type of vasculitis, i.e., polyarteritis nodosa (Figure 2).

3. Multisystem disease

Like other immune complex diseases, vasculitis may involve any organs of the body since almost all organs are supplied by blood vessels. However, as will be discussed later, certain vasculitides may have a predilection for certain sizes and sites of blood vessels.

Table 2 lists some of the clinical manifestations of leukocytoclastic venulitis (LCV), which is the most common type of vasculitis. Postcapillary venules of the superficial dermis are commonly involved, resulting in the characteristic palpable purpura as mentioned previously. Other types of skin lesions

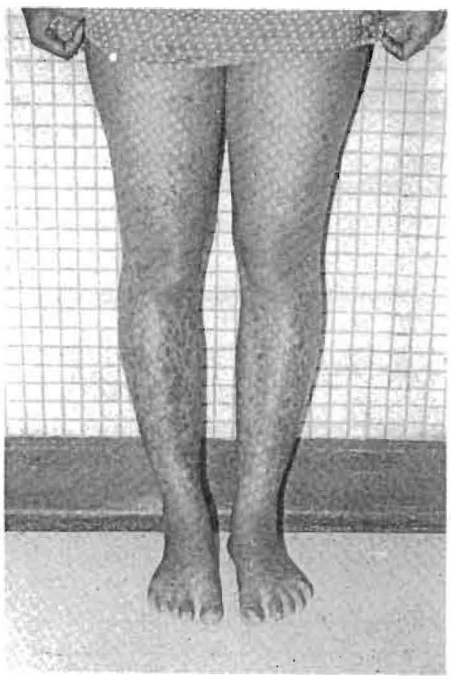

Fig. 1 Palpable purpura in a patient with leukocytoclastic venulitis (LCV).

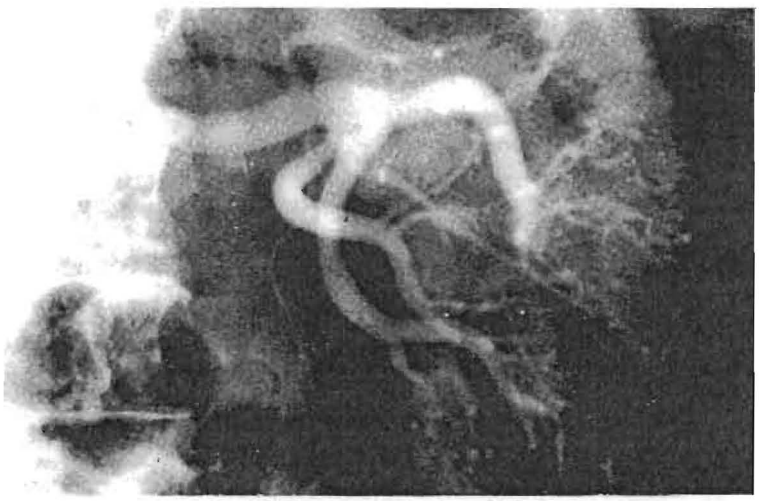

Fig. 2 Renal microaneurysms in polyarteritis nodosa (PAN).

Table 2. Clinical manifestations of leukocytoclastic venulitis (LCV)

1. Systemic: fever, weight loss
2. Cutaneous: palpable purpura, urticaria, erythematous maculopapular rash, vesicle, livedo reticularis, necrosis, gangrene, ulceration
3. Musculoskeletal: arthralgia, arthritis, myositis
4. Renal: proteinuria, haematuria, renal failure
5. Gastrointestinal: abdominal pain, GI bleeding
6. Neurologic: encephalopathy, neuropathy
7. Pulmonary: Pneumonitis, pleural effusion
8. Cardiovascular: myocarditis, pericarditis

may also occur but none is as pathognomonic as palpable purpura. LCV could be found in selected cases of chronic urticaria,[12,13] although controversy concerning this still exists.[14] We found that vasculitis was a common histological feature in chronic urticaria without any clinical or prognostic significance.[14] Gastrointestinal involvement was more common in young LCV patients than in older ones.[15] The manifestations could be abdominal pain, nausea, vomiting, gastrointestinal bleeding and diarrhoea. The authors also point out that acute abdomen in LCV, as a rule, was the medical acute abdomen, whereas in cases of polyarteritis nodosa, it was mainly the surgical type necessitating exploratory laparotomy and resection of the infarcted bowels.[15]

Table 3. Clinical manifestations in 19 patients with PAN

Manifestation	Number of patients	Total number and per cent of total
Respiratory		14 (74%)
Pulmonary infiltrates	8	
Wheezing	6	
Cough and dyspnoea	4	
Haemoptysis	3	
Pleural effusion	3	
Sinusitis and nasal ulcer	2	
Renal		13 (68%)
Azotaemia/↓CrCl	13	
Abnormal urinary sediment	9	
Proteinuria	7	
Positive renal arteriogram	4/6	
Musculoskeletal		10 (53%)
Arthralgia-arthritis	7	
Myalgia	6	
Hypertension		9 (47%)
Constitutional symptoms		9 (47%)
Fever	7	
Weight loss	3	
Gastrointestinal		9 (47%)
Hepatomegaly/abnormal LFT	7	
GI bleeding	6	
Abdominal pain	3	
Diarrhoea	1	
Neurological		8 (42%)
Neuritis	7	
Headache	2	
Seizure	1	
Cardiac		7 (37%)
Congestive failure	7	
Pericarditis	1	
Skin-mucous membrane		6 (32%)
Orogenital ulcers	2	
Ill-defined rash	2	
Palpable purpura, urticaria, nodule, papulovesicle	1 each	

The clinical manifestations of 19 patients with polyarteritis nodosa (PAN) seen at the University of Colorado Medical Center are listed in Table 3.[1] It is important to point out that in 17 of the 19 patients or 84 per cent of the total, three or more systems were involved, counting constitutional symptoms of fever and weight loss as one system. The presenting symptoms and signs of these 19 patients as shown in Table 4 illustrate the main complaints of PAN patients: mononeuritis multiplex, prolonged fever and unexplained weight loss. One case of progressive PAN disclosed during a routine investigation of a young Thai woman with severe hypertension was recently recorded.[16]

II. Confirmation and identification of vasculitis types

1. Histopathologic confirmation

Although certain types of vasculitis can be diagnosed visually, such as the palpable purpura in leukocytoclastic venulitis, pathological confirmation is nevertheless frequently sought, particularly in academic medicine. The points to be considered when examining a section of vasculitis lesion, are the size of the blood vessel involved (i.e. aorta, artery, vein or post-capillary venule) and the type of inflammation seen (i.e., necrotizing vs granulomatous inflammation). These considerations form the basis of Zeek's pathological classification of vasculitis in 1953.[17] In 1978, we at the University of Colorado Medical Center, constructed a scheme of classification as shown in Table 5.[1] It is based on Zeek's time-honoured classification, but includes in a single scheme clinical, pathogenetic, aetiologic and therapeutic classifications. It is important to emphasize here that overlaps of various vasculitides may occur.[18,19] Yet it is still essen-

Table 4. Presenting symptoms and signs in 19 patients with polyarteritis nodosa.

Symptoms and signs	Number of patients and per cent of total
Mononeuritis multiplex and polyneuritis	7 (37%)
Constitutional symptoms (fever, weight loss)	4 (21%)
Arthralgia-arthritis	3 (16%)
Skin rash (nodules, papulovesicles)	2 (11%)
Pleurisy and haemoptysis	1 (5%)
Abdominal pain	1 (5%)
Nephrotic syndrome	1 (5%)

tial to keep this classification scheme in mind since it reminds one about the diagnosis, the aetiologic factors one should look for and the most effective treatment to be chosen for that type of vasculitis.

Figure 3 illustrates the histopathology of an LCV lesion. Characteristic features are mural neutrophilic infiltration of postcapillary venules, leukocytoclasis or nuclear dust, fibrinoid necrosis, endothelial swelling and extravasation of red blood cellss. Soter et al[20] believed that neutrophilic and lymphocytic vasculitis were two separate entities. The former was frequently associated with hypocomplementaemia and positive immunofluorescence whereas these were lacking in lymphocytic vasculitis. Instead, we feel that both neutrophilic and lymphocytic vasculitis are within the spectrum of the same disease but at different developmental stages. This conclusion is based on the observation that both neutrophilic and lymphocytic types of vasculitis could be seen in the same patient if biopsies of two morphologically different lesions were either taken simultaneously or some days apart.[1,21] In addition, the incidence of vascular deposition of immunoreactents (immunoglobulins and/or complement) was not different in either type of vasculitic lesion.[1,21]

The histopathology of polyarteritis nodosa is shown in Figure 4. Infiltration of the inflammatory cells, particularly neutrophils, in all layers of the small- and medium-sized arteries is the characteristic finding. This is generally accompanied by hyaline necrosis of the media, swelling of the intima, disruption of the internal elastic lamina and muscularis mucosae. This results in weakening of the vascular wall, bulging and aneurysmal dilatation . Vascular thrombosis, periarterial fibrosis and recanalization are the changes which occur in the late stage (Figure 5). Different stages of inflammation may be seen at different levels of the same artery, i.e., segmental involvement. Therefore, multiple levels of sectioning and multiple biopsies are essential. In addition, biopsies of asymptomatic organs or tissues, particularly the testicles and muscles, may prove useful in a great number of polyarteritis nodosa patients with unexplained fever and weight loss.[22]

Figure 6 illustrates the necrotizing granuloma and giant cell formation seen in Wegener's granulomatosis.

2. Immunopathologic confirmation

Immunopathologic studies of vasculitis lesions are mainly of academic interest rather than of diagnostic importance. If positive, they confirm the diagnosis of immune complex vasculitis but this does not rule out the presence of the disease if the studies are negative. Table 6 gives the frequency of positive vascular deposition of immunoreactants in various cellular types of cutaneous venulitis.[1] The overall incidence was 69 per cent. C_3 was found most frequently, followed in frequency by IgM and IgA. IgG and fibrin were present in only a few biopsy specimens. The immunoreactants were seen as granular deposits along the post-capillary venules of dermal papillae and superficial dermis (Figure 7).

Skin immunofluorescence was more informative in certain cases of vasculitis in which the pathologic studies of the lesion were negative i.e., while the immunofluorescent study may be positive, the histopathologic picture may show only perivascular mononuclear cell infiltra-

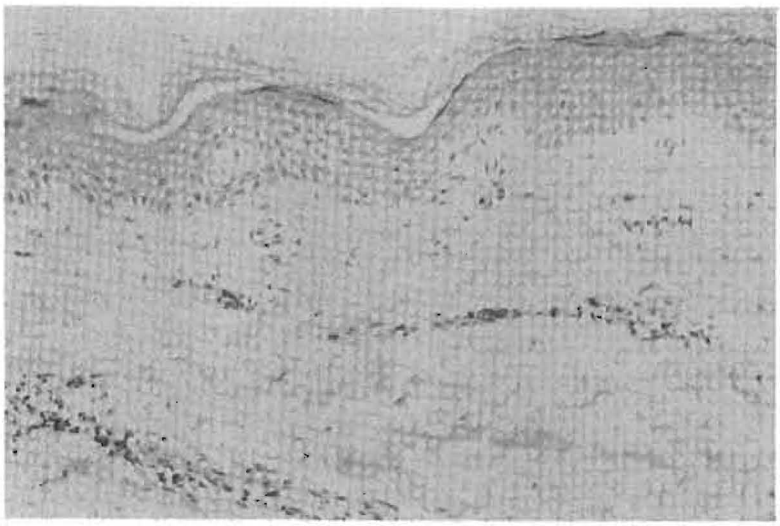

Fig. 3 Histopathology of leukocytoclastic venulitis showing infiltration of neutrophils and nuclear dust within and around vessel wall of superficial dermis.

Table 5. Vasculitis classification at the University of Colorado Medical Center.

	Polyarteritis nodosa	Allergic granulomatosis	Wegener's granulomatosis	Cutaneous venulitis	Termporal arteritis
Synonyms	Periarteritis nodosa	–of Churg and Strauss	. . .	Leukocytoclastic vasculitis Henoch-Schönlein purpura Hypersensitivity angiitis	Giant cell arteritis
Variants	Mucocutaneous lymph node syndrome (Kawasaki disease) Cutaneous (limited) PAN	. . .	. . .	. . .	Takayasu's arteritis (pulseless disease) Polymyalgia rheumatica
Pathologic features	Muscular arteries; necrotizing inflammation	Muscular arteries; necrotizing inflammation with granuloma	Muscular arteries, arterioles and veins; necrotizing inflammation with granuloma	Postcapillary venules; necrotizing inflammation	Large and medium arteries; granuloma
Clinical features	Widespread, lungs also involved	Widespread, wheezing and eosinophilia	Widespread but common to upper and lower respiratory tract and kidneys	Widespread but common to skin, joint, serosa and kidneys	Aorta and its main branches
Evidence for immune complex pathogenesis	Probable	None	Possible	Definite	Possible
Etiologic association					
Other connective tissue diseases (Sle, RA, etc)	Yes	None	None	Yes	None
Specific infections	Hepatitis B Otitis media (?)	None	None	Hepatitis B Infectious mononucleosis Histoplasmosis Gonococcaemia Bacterial endocarditis	None
Drugs	Amphetamine Sulfonamides Penicillin	None	None	Sulfonamides Penicillin	None
Preferred treatment	Corticosteriod and cyclo-phosphamide	Corticosteroid	Cyclophosphamide	Observation, ? corticosteriod or cyclophosphamide	Corticosteriod

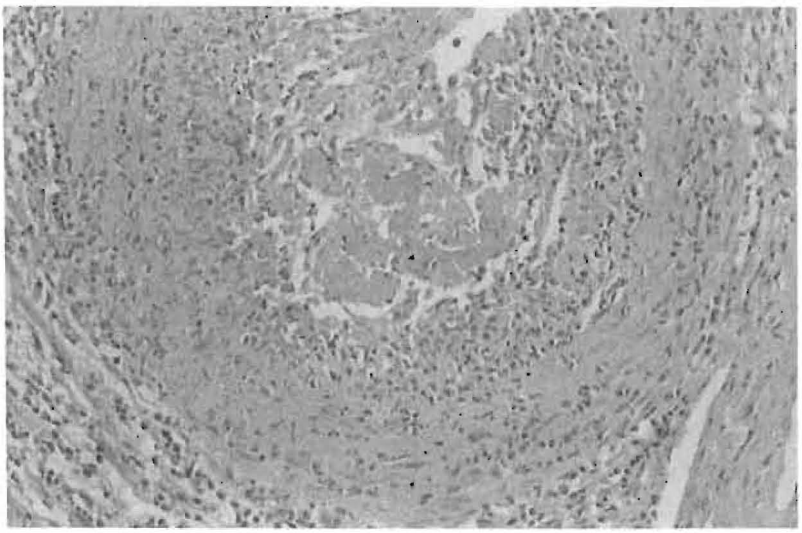

Fig. 4 Histopathology of polyarteritis nodosa. The entire arterial wall is infiltrated by acute inflammatory cells, accompanied by fibrinoid necrosis.

Fig. 5 Late or healing stage of the arteritis. Vascular thrombosis, periarterial fibrosis and recanalization are the prominent histopathologic features.

Table 6. Frequency of positive vascular deposition of immunoreactants in various cellular types of cutaneous venulitis.

Cellular types of cutaneous venulitis	Number positive by IF compared with number examined	Per cent positive IF
Neutrophilic ("acute")	27/34	79
Mixed neutrophilic and lymphocytic ("subacture")	10/20	50
Lymphocytic ("chronic")	4/5	80
Over all	**41/59**	**69**

tion because of late biopsy. In addition, normal skin from vasculitis patients also showed vascular deposition of immunoreactants in 27 out of 51 biopsy specimens (53 per cent of the total).[1] This was helpful in diagnosing patients with post-vasculitis nephritis who did not have skin lesions at the time of kidney biopsy. In five of the 11 such patients immunofluorescent studies of their normal skins were positive, a 45 per cent yield, thus confirming the aetiology of their nephritis.[1] Another useful aspect of immunofluorescent study is that it can identify the suspected aetiologic agents, such as HB_s Ag or others, responsible for a particular case of vasculitis.

3. Radiographic confirmation

As mentioned earlier, coeliac axis (renal, hepatic, superior mesenteric and splenic arteries) angiography may be helpful in the diagnosis of PAN if multiple microaneurysms are found (Figure 3). This was the leading clue in diagnosing PAN in a hypertensive patient when the causes of her hypertension were being investigated.[16] Renal arteriograms have been reported to be positive in about 50-67 per cent of PAN patients.[1] Similarly, fluorescein angiography is helpful in diagnosing retinal vasculitis; aortogram, in diagnosing Takayasu arteritis. The disappearance of the microaneurysms after appropriate treatment may be the result of successful treatment or it may be due to occlusive thrombosis, rupture or poor opacification of the aneurysms as a result of decreased renal blood flow.[23] In addition to angiographic study, radiographic studies of the chest and the paranasal sinuses may aid in the identification of certain types of vasculitis particularly Wegener's granulomatosis.[5,8]

III. Supportive laboratory evidence

At times, tissue and radiographic diagnoses may be non-diagnostic or unfeasible. One then has to search for other supportive evidence of vasculitis such as eosinophilia, high

erythrocyte sedimentation rate, abnormal urinalysis or impaired renal functions, hypocomplementaemia, cryoglobulinaemia and the presence of circulating immune complexes. Although these laboratory findings are non-diagnostic for vasculitis, they provide supportive evidence for the clinical impressions. The laboratory findings in 79 patients with leukocytoclastic venulitis and 19 patients wth polyarteritis nodosa, who were seen at the University of Colorado Medical Center, are summarized in Table 7.[1] Whenever posible, it is suggested that the following laboratory tests should be done during the diagnostic work-up of a patient with vasculitis, namely, complete blood count, platelet count, urinalysis, ESR, muscle enzymes, renal and liver function tests, HBsAg, complement profiles, cryoglobulins and circulating immune complex levels

IV. Identification and removal of the aetiologic agents (if found)

In most cases the cause of vasculitis is unknown. Table 8 is a partial list of the conditions occasionally associated with leukocytoclastic venulitis and polyarteritis nodosa.[1,3,4] Some might be chance association although some were the real causes since the causative agents could be identified in the affected blood vessels and/or the vasculitis was cured by removing the causative agents. Examples showing these two sides of the story are abundant in the literature. For example, we have recorded a case of LCV with EDTA-induced pseudothrombocytopenia[24] and another case with polymyositis and Waldenström's macroglobulinaemia.[25] These may be purely chance associations. In addition, we have encountered six patients among 20 consecutive cases with PAN who had undergone allergic hyposensitization shortly before the onset of PAN (Figure 8).[26] The association was too pronounced to be simply a chance association, although we could not prove the cause-effect relationship. On the

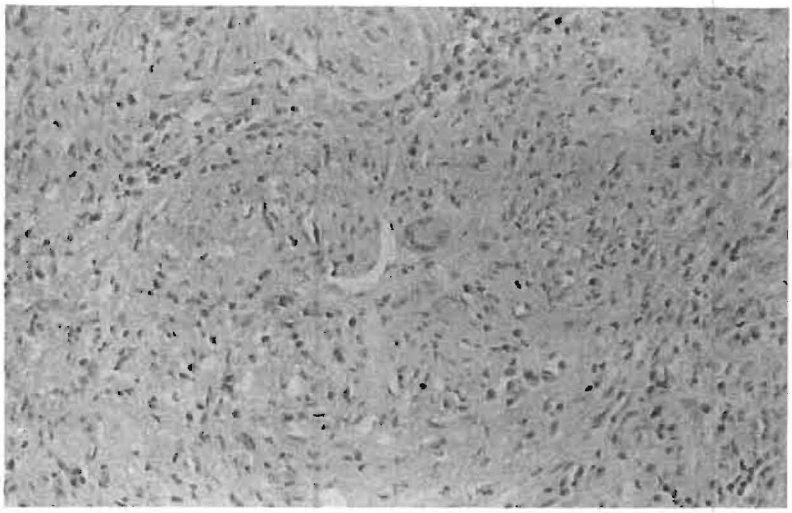

Fig. 6 Histopathology of Wegener's granulomatosis showing necrotizing inflammation together with formation of granuloma.

Fig. 7 Immunofluorescent finding in an LCV lesion showing granular deposits of IgM around the superficial dermal vessels.

Table 7. Laboratory findings in patients with leukocytoclastic venulitis (LCV) and polyarteritis nodosa (PAN) seen at the University of Colorado Medical Centre.[1]

Laboratory findings	LCV (Number = 79)		PAN (Number = 19)	
	Number	%	Number	%
Anaemia	16	20	7	37
Leukocytosis	6	8	5	26
Eosinophilia	14	18	6	32
↑ ESR	42	60	9	47
↑ IgE	14	25	7	39
HBsAg	5	6	4	21
↓ Renal function	42	53	13	68
Cryoglobulinaemia	43	54	9	47
Hypocomplementaemia	23	29	8	42
↑ Clq binding (immune complexes)	46	58	10	53

Table 8. Partial list of the conditions occasionally associated with leukocytoclastic venulitis and polyarteritis nodosa.

1. Rheumatic diseases: SLE, rheumatoid arthritis, dermatomyositis, essential cryoglobulinaemia and Sjogren's syndrome
2. Infection: bacterial endocarditis, disseminated gonococcaemia, meningococcaemia, hepatitis B, infectious mononucleosis and histoplasmosis
3. Malignancy: multiple myeloma, Waldenstrom's macroglobulinaemia, lymphoma and carcinoma
4. Hypersensitivity: serum sickness and drug reaction
5. Complement deficiency: C1q and C2 deficiency
6. Miscellaneous: serous otitis media, drug abuse, allergic hyposensitization, regional enteritis and chronic ulcerative colitis
7. Idiopathic

other hand, infectious agents such as HBsAg could be identified in the affected blood vessels either immunologically or electronmicroscopically[27] and the resolution of the vasculitis could be observed when the causative infectious agents were treated or cleared,[28] thus indicating direct cause and effect. Apart from LCV and PAN, the cause or the association of other types of vasculitides have rarely been reported.

Aware of the possible causes or associations of vasculitis as previously described, one should include the following investigations during the diagnostic investigation in order to determine the cause of the patient's vasculitis:

1. A careful history and thorough examination with particular attention to the history of drug intake, chemical exposure, symptoms and signs of infection and collagen vascular diseases, unexplained fever or weight loss.

2. Haemoculture or culture from appropriate sites for bacteria and fungus.

3. HB_SAg and other viral cultures or viral serology as indicated.

4. Antinuclear factor and rheumatoid factor.

5. Total haemolytic complement activity (CH_{50}) and individual complement concentration if CH_{50} is low.

6. Cryoglobulins.

7. Other appropriate studies such as radiography, bone marrow aspiration, etc., when malignancy is suspected.

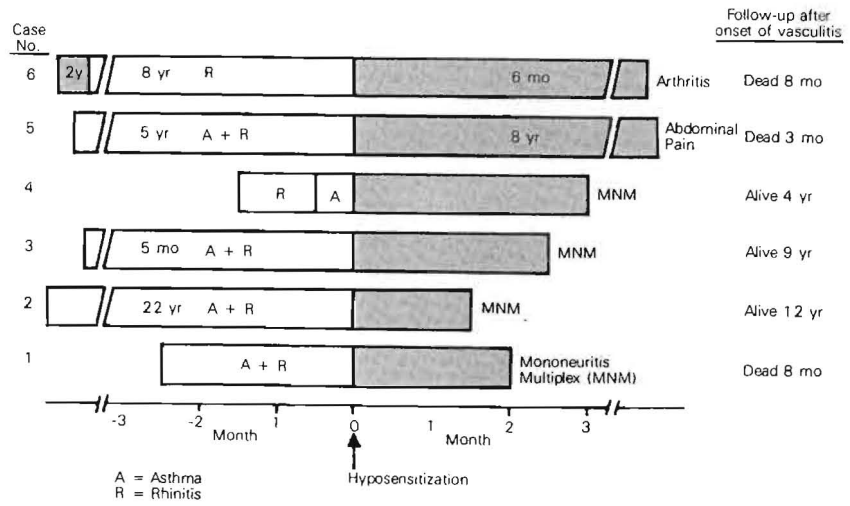

Fig. 8 Occurrence of PAN in six patients, shortly after five of them received hyposensitization for their allergic bronchial asthma.

V. Clinical staging

Once the diagnosis of vasculitis is confirmed, a physician must establish which organs are involved by the vasculitis process. This is essential in order to formulate treatment regimens. It is also helpful in determining the prognosis and serves as the baseline for future follow-up of the patient. Basic clinical staging should include a careful history and physical examination, urinalysis, renal and liver function tests, stool examination for occult blood, chest radiography and an electrocardiogram. When indicated, the following tests may be done: electromyography, nerve conduction study, lumbar puncture, intravenous pyelography, radiography of the GI tract, liver scan, appropriate angiography, muscle and kidney biopsies, among others.

VI. Treatment

What treatment to be prescribed for a vasculitis patient depends on the following factors:

i) What type of vasculitis that the patient has,

ii) Which major organs have been involved,

iii) What treatment has proved effective for that type of vasculitis at that particular stage of clinical involvement,

iv) How acute or chronic the disease is,

v) Whether the patient has any concurrent medical problem such as concurrent infection which may influence the therapeutic judgement, and

vi) Whether the cause of the patient's vasculitis is known.

The following points about the treatment of vasculitis may be made:

1. Treat or remove the underlying cause such as drugs, insecticides, infections and malignancies. Any drug can cause vasculitis, particularly antibiotics, sedatives and thiazides. Vasculitis in SLE may be adequately

controlled with antimalarial drugs while vasculitis associated with inflammatory bowel disease can be controlled with sulfapyridine.[29]

2. The administration of corticosteroids in moderate doses (e.g. 40 mg/day of prednisone) is universally accepted as an effective treatment for giant cell arteritis.[30] No additional immunosuppressive agents are needed to treat this condition. However, it is generally recommended the administration of corticosteroids be slowly and carefully tapered off in order to prevent relapse and blindness.[29-30]

3. Allergic granulomatosis of Churg and Strauss is another one of the vasculitides which responds very well to corticosteroids.[7] Long-term survivors have been observed among our patients receiving just enough low-dose, alternate-day corticosteroids to control their asthma symptoms (unpublished data).

4. Cyclophosphamide is now accepted as the treatment of choice for Wegener's granulomatosis.[2] A daily dose of 1-2 mg/kg is recommended at the initiation of treatment; an increase in this dose of 25 mg every two weeks is recommended if no favorable response is observed or until the leukocyte count drops below 3,000/mm^3 or until other complications develop. A higher initial dose of cyclophosphamide may be needed to control fulminant, progressive diseases. Short-term corticosteroids may be of benefit in patients with severe cutaneous, eye and serosal vasculitis.[2]

5. For decades, corticosteroid therapy has been the mainstay for the treatment of polyarteritis nodosa. Its efficacy has been confirmed, although long-term treatment is needed.[31] For patients who do not respond to corticosteroids, immunosuppressive agents, particularly cyclophosphamides, may be added; this combination will generally induce remission.[1,2] The current trend indicates that cyclophosphamide therapy may ultimately become the treatment of choice in PAN.[32]

6. Treatment of leukocytoclastic venulitis (LCV) is a most controversial and complicated issue. Palpable purpura in certain cases may be mild and self-remitting. Lesions may resolve after bed rest, leg elevation or wearing elastic stockings. Corticosteroids have been frequently used in the treatment of LCV especially when the skin lesions are extensive or associated with musculoskeletal symptoms. However, we found that they were not universally effective and that high doses were usually required. Corticosteroids were found effective in ameliorating the symptoms of acute abdomen in LCV[15] but inadequate in reversing or arresting the renal involvement of LCV.[29] Lately we have shared the experience of others[29,33] that dapsone in daily doses of 100 mg is very effective in controlling the cutaneous manifestations of LCV. Colchicine and indomethacin also have been found beneficial in some cases of LCV.[34,35] Immunosuppressive agent are reserved for severe cases of LCV with renal, pulmonary and cerebral involvement although no controlled studies have been done.

VII. Follow-up

Follow-up is an important step in the care of vasculitis patients. A change in therapeutic regimens relies on clinical and laboratory data. The erythrocyte sedimentation rate seems to be one of the good indicatiors of disease activity. It is important to realize that visceral organ involvement, particularly glomerulonephritis, may progress despite the resolution of cutaneous signs. Therefore, it is essential to perform urinalysis during each follow-up visit; full-scale renal and liver function tests should be repeated periodically and the results compared with previous studies. Aggressive treatment should be promptly started if signs of new organ involvement are uncovered.

PATHOGENESIS

Any discussion of vasculitis can not be considered complete without a few words about its pathogenesis. Immune complex pathogenesis is firmly established in LCV and PAN. This is based on the occurrence of vasculitis lesions in well-known immune complex-mediated diseases such as SLE and rheumatoid arthritis as well as the characteristic vascular deposits of the immunoreactants in both lesions and normal skin. Increased vascular permeability induced by the intradermal injection of histamine into the normal skin of LCV patients can lead to the pathologic change of vasculitis in the skin.[36] This clearly indicates that tissue injury can follow vascular deposition of immunoreactants. However, immune complex pathogenesis is less well established in other types of vasculitides. Other mechanisms of immunologic tissue injury such as IgE-mediated (type I) reaction, direct vascular injury (type II) and cell-mediated immunologic (type IV) injury have also been proposed for the pathogenesis of various vasculitides, however, direct support for these mechanisms is lacking.[37]

In addition to the aforementioned immune mechanisms, some nonimmunologic factors may also contribute to the pathogenesis or the perpetuation of vasculitis. Examples of such nonimmunologic factors include C-reactive protein,[38] a tissue plasminogen activator,[39] as well as some cytotoxic serum factors; how they interact with the immune mechanisms in the pathogenesis of vasculitis remains to be investigated.

CONCLUSION

Vasculitis is an immune complex-mediated vascular inflammation. Diagnosis is mainly a pathologic diagnosis although this may at times be impossible, at least antemortemly, in cases such as retinal vasculitis. Diagnosis of vasculitis is analogous to the diagnosis of anaemia in the sense that it does not imply the type of anaemia and its cause. Therefore, it is the responsibility of the physician to establish the type and cause of his patient's vasculitis.

The guidelines given in this paper should provide an effective and practical approach in the diagnosis and management of vasculitis.

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