ISSN: 2091-2749 (Print)
2091-2757 (Online)

Correspondence
Dr. Buddhi Prasad Paudyal
Department of Medicine
Patan Academy of Health Sciences, Lalitpur, Nepal
Email: buddhipaudyal@pahs.edu.np

Peer Reviewed By
Dr. Nabees Man Singh Pradhan
Patan Academy of Health Sciences

Peer Reviewed By
Dr. Jay N Shah
Patan Academy of Health Sciences

Clinical characteristics and outcome of vasculitides

Buddhi Prasad Paudyal,[1] Madhu Gyawalee[2]

[1]Associate Professor, Department of Medicine, [2]Lecturer, Department of Dermatology, Patan Academy of Health Sciences, Lalitpur, Nepal

ABSTRACT

Introductions: Vasculitides can cause significant morbidity and mortality if not treated on time. There is lack of data locally. This study aims to define the pattern, clinical characteristics, and outcome of vasculitides.

Methods: This was a cross sectional study between January 2011 and December 2015 at Patan Hospital, Patan Academy of Health Sciences, Lalitpur, Nepal. The medical records of patients diagnosed with vasculitides in adults rheumatology service of the hospital were reviewed.

Results: Ninety six patients were diagnosed with vasculitides during the study period. The mean age was 42.2 years. Sixty nine (71.8%) patient had small vessel, 20 (20.8%) large vessel and five (5.2%) had variable vessel vasculitides. Seventy five patients (78.1%) had primary and 21 (21.8%) secondary vasculitides. Cutaneous leucocytoclasticangitis was seen in 27 (28.1%), Takayasu arteritis in 17 (17.7), Henoch-Schonlein purpura in 11 (11.4%) and Rheumatoid arthritis associated vasculitis in nine patients. Purpura was present in all 96 (100%). The overall mortality was 9 (9.3%).

Conclusions: Primary vasculitides were more common than secondary forms. Small vessel vasculitis was the most common. Cutaneous symptoms were predominant features. The mortality was attributed to active disease, sepsis, and complications of the primary disease.

Keywords: Clinical characteristics, outcome, vasculitis, Patan Hospital, Nepal

INTRODUCTIONS

Vasculitides are a heterogeneous group of diseases defined by the presence of inflammatory infiltrates in the blood vessel walls. Spread over several entities, these are rare but important clinical conditions. Timely identification and treatment can significantly decrease the associated morbidity and mortality.[1]

Epidemiological data on vasculitides are mostly from Western countries. In Europe, the annual incidence of primary systemic vasculitides is approximately 20 per million population.[2] Studies have showed that vasculitides are common in elderly; however, the prevalence differs in different populations. In Western Nepal, only one case of vasculitis was observed in a series of 365 rheumatic cases.[3]

Except few case reports and small series[4,5] on vasculitis, there is lack of data on clinical presentation and outcome locally. This study aims to assess clinical characteristics and outcome of vasculitic diseases from a tertiary care teaching hospital in Kathmandu, Nepal.

METHODS

This was a cross sectional study conducted at Patan Hospital, Patan Academy of Health Sciences (PAHS), Lalitpur, Kathmandu, Nepal. The medical records of patients diagnosed with vasculitides in the adult rheumatology service (medical outpatient and different wards) of Patan Hospital from 1st January 2011 to 31st December 2015 were reviewed. Patient's demographic data and clinical information on type and subtype of vasculitides, presentation, laboratory, imaging and biopsy, treatment, and outcome until the last follow up of few days to a maximum of 4 years were recorded. Investigations and imaging studies included were: rheumatoid factor (RF), antinuclear antibody (ANA), anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibodies, antineutrophil cytoplasmic antibodies (c-ANCA & p-ANCA), serological tests for hepatitis B, hepatitis C, human immunodeficiency virus (HIV), and angiogram of the aorta/affected blood vessels in selected patients. Children below 14 years of age were excluded. For primary vasculitides, the diagnosis was based on American College of Rheumatology (ACR) 1990 vasculitis classification criteria[6] and Chapel Hill Consensus Conference 1992 vasculitis nomenclature system.[7] For secondary vasculitides, diagnosis was based on clinical manifestations supported by appropriate investigations. Patients were treated according to the standard treatment protocol for that particular type of vasculitis[8,9] and followed up every 3 to 6 months. Outcome at last follow up was recorded. A broad outcome measure was used, which is also used for childhood systemic lupus erythematosus.[10] The outcome was grouped as remission on treatment, active disease despite treatment, lost to follow up, and death. The death at home or other health facility was confirmed by interrogating with the family members or relatives. Ethical approval was taken from Institutional Review Committee of PAHS. SPSS was used for descriptive analysis.

RESULTS

There were 96 patients diagnosed with vasculitides during the study period. Mean age was 42.2 years (range 18-78). Female to male ratio was 2:1. Sixty-nine (71.8%) patients had small vessel, 20 (20.8%) large vessel, five (5.2%) variable vessels and two (2%) had medium vessel involvement. Primary vasculitides was present in 75 (78.1%) and secondary in 21 (21.9%), (Table 1). Clinical manifestations of vsaculitis presented varyingly, Table 2.

The outcome was good in 37 (38.5%) cases, (Table 3). Mortalities in primary vasculitides were one (1%) case each of Takayasu arteritis and Wegener's granulomatosis; and one (1%) case each of polyarteritis nodosa and microscopic polyangiitis. Among secondary vasculitides, mortalities were all two (2%) cases of malignancy associated and one (1%) case of lupus associated mesenteric vasculitis.

Table 1. Frequency distribution of vasculitic disorders at Patan Hospital

		Type	Male	Female	Mean age y
Large vessel vasculitis (n= 20)		Takayasu arteritis (17)	2	15	30.71
		Gaint cell arteritis (3)	1	2	71.33
Medium vessel vasculitis (n= 2)		Polyarteritis nodosa (2)	1	1	45
Small vessel vasculitis (n=69)	Primary (48)	Wegener's granulomatosis or granulomatosis with polyangiitis (7)	3	4	55.29
		Churg-Strauss syndrome (2)	1	1	41
		Microscopic polyangiitis (1)	1	0	57
		Henoch-Schonlein purpura or IgA vasculitis (11)	6	5	32.45
		Cutaneous leucocytoclastic angiitis (27)	9	18	43.3
	Secondary (21)	Rheumatoid arthritis associated (9)	2	7	58.11
		Systemic lupus erythematosus associated (6)	0	6	27.83
		Malignancy associated (2)	2	0	66.5
		Drug associated (4)	3	1	43.75
Variable vessel vasculitis (n=5)		Behcet's disease (5)	2	3	35

Table 2. Common manifestations of some forms of vasculitides

Diagnostic category (n)	Presenting features	Number (%)
Takayasu arteritis (17)	Loss of pulses	16(94%)
	Arthritis/arthralgia/myalgia	16 (94%)
	Fever	8 (47%)
	Hypertension	8 (47%)
	Headache	4 (24%)
	Stroke	2 (12%)
Wegener's granulomatosis (7)	Eye inflammation*	6 (86%)
	Arthritis/arthralgia/myalgia	6 (86%)
	Nasal/Paranasal symptoms †	5 (71%)
	Fever	5 (71%)
	Renal manifestations ‡	5 (71%)
	Pulmonary features §	5 (71%)
	Neuropathy	5 (71%)
	Purpura	2 (29%)
Henoch-Schonlein purpura (11)	Purpura	11 (100%)
	Arthritis/arthralgia/myalgia	11 (100%)
	Abd. Pain/GI bleeding	5 (45%)
	Renal manifestations ‡	4 (36%)
Cutaneous leucocytoclastic angiitis (27)	Purpura	27 (100%)
	Arthritis/arthralgia/myalgia	10 (37%)

Note: *Eye inflammation: scleritis, keratitis, proptosis, scleromalacia; † Nasal/paranasal symptoms: sinusitis, epistaxis, nasal septum perforation, nasal crusts;‡ Renal symptoms: haematuria, proteinuria, elevated creatinine;§ Pulmonary symptoms: haemoptysis, infiltrates/cavities/nodules on x-ray or CT scan

Table 3. Clinical outcome of vasculitides (n=96)	
Outcome	**Number (%)**
Disease remission while on treatment	37 (39%)
Active disease despite treatment	15 (16%)
Lost to follow up	35 (36%)
Death	9 (9%)

DISCUSSIONS

In this study mean age of the patients with vasculitis was 42 years. Vasculitis, being a broad constellation of disorders, is a disease of all age groups. Different forms of vasculitides have different age predilection. Primary vasculitides like Takayasu arteritis and Henoch-Schonlein purpura are more common in young age group whereas most of the other forms of primary systemic vasculitides, particularly Giant cell arteritis are more common with advancing age.[11] The relative lower mean age in this series could be due to predominance of Takayasu arteritis, cutaneous leucocytoclastic angiitis and Henoch-Schonlein purpura which are all more common in young age group and at the same time, relative rarity of other forms of primary vasculitides which are more often seen in elderly.

There was female predominance (male:female ratio of 1:2), and more so for diseases like Takayasu arteritis, cutaneous leucocytoclastic angiitis, and secondary vasculitides associated with autoimmune diseases like RA and SLE. Similar female predominance in different types of vasculitides is reported from India.[12,13] In this study, primary vasculitis was more common than secondary vasculitis in general, 78% versus 22% respectively in both sexes.

The most common form of vasculitis in our study was cutaneous leucocytoclastic angiitis, followed by Takayasu arteritis, Henoch-Schonlein purpura, and RA associated secondary vasculitis. Cutaneous vasculitis was also a predominant form of vasculitis in studies from Western India[13] and Denmark.[14] The relative excess of Takayasu arteritis over other primary vasculitides may be due to the fact that this disease is more prevalent in Asian countries.[15] Henoch-Schonlein purpura is predominantly a disease of childhood; however, several studies have observed that this disease also comprises significant proportion of vasculitis in adult population.[6,12] Other forms of systemic vasculitides, particularly Giant cell arteritis, Polyarteritis nodosa, Churg-Strauss syndrome, and Microscopic polyangiitis were less common as in other series.[12,16] Behcet's disease, which can affect veins in preference to arteries and can affect all sizes of blood vessels, was observed in five patients (5.2%) in our study. The relative rarity of Behcet's disease in our series as compared to Indian[12] and Iranian studies[16] could either be due to rarity of this disease in our population or due to lack of referral to rheumatology service.

Takayasu arteritis often causes granulomatous inflammation of the aorta and/or its major branches and more often begins before the age of 50 years.[17] The most common way of presentation in our population was muscle and joint pain and lack of pulses on physical examination, in 94% of cases. Approximately half (47%) presented with hypertension, whereas two cases developed stroke as a complication of the disease. Takayasu arteritis is the commonest cause of renovascular hypertension in India,[18] so early identification and treatment to optimal level is essential to avoid complications of hypertension like stroke and myocardial ischaemia.

Many cases of Wegener's granulomatosis in our series had diffuse disease and presented with multisystem involvement including kidneys. One patient underwent renal transplantation for end-stage kidney disease. Relapse of disease was seen in three cases; one patient had multiple relapses. She had bilateral parotid enlargement as part of relapse before she died of severe sepsis. Though ours was a small series and not directly comparable with data from larger series, the relapse in treated Wegener's granulomatosis is as high as 57%.[19]

Both Henoch-Schonlein purpura and cutaneous leucocytoclastic angiitis presented with purpuric rashes in 100% of cases. In Henoch-Schonlein purpura, renal involvement in the form of haematuria and proteinuria was observed in almost half of the patients whereas gastrointestinal involvement was seen in 36% of cases. Several other studies have also highlighted that Henoch-Schonlein purpura is more severe in adults particularly with renal involvement.[20]

As we were dealing with several different types of vasculitides, we used a broad outcome measures which has also been used for childhood systemic lupus erythematosus.[10] More than one third of our patients lost to follow up. It appeared that many patients with milder forms of the disease particularly cutaneous vasculitides lost to follow up. Nine patients died in this series; two each from Wegener's granulomatosis, Takayasu arteritis and malignancy associated secondary vasculitis; and one each from Polyarteritis nodosa, SLE and Microscopic polyangiitis. In Wegener's granulomatosis, one patient died of active disease whereas another succumbed to severe sepsis. In Takayasu arteritis, one patient died due to acute left ventricular failure due to uncontrolled hypertension, whereas the cause of death was not clear in the second who died at home. In malignancy associated vasculitis, the cause of death was terminal cancer. In all other cases, the death was due to active vasculitis.

As different forms of vasculitides present, with different manifestations, to different sub-specialists, only patients seen in rheumatology service were included in this study. Thus, some form of vasculitides like renal-limited vasculitis and primary central nervous system vasculitis could have been missed, whereas others like Behcet's disease could have been under represented. Similarly, as this study was conducted in patients older than 14 years of age, vasculitis presenting exclusively in childhood, particularly Kawasaki disease was not observed in this study.

Through this study, we have tried to provide a bird's eye view of vasculitis scenario from a hospital in central Nepal. Being a single centre report of retrospective design and with small sample size, this study may not reflect the true picture of the extent and problem of vasculitides in Nepal. Nevertheless, we believe that this study will open up avenues for future research and on that ground more comprehensive vasculitis database and prospective studies can be planned in the future.

CONCLUSIONS

Primary vasculitides were more common than secondary forms of vasculitides in general and in both the sexes. Small vessel vasculitis was the most commonly observed form of vasculitides; cutaneous leucocytoclastic angiitis, Henoch-Schonlein purpura, and autoimmune disease associated secondary vasculitides were more frequent presentations. Purpura was the most frequent presentation in cutaneous leucocytoclastic angiitis and Henoch-Schonlein purpura whereas other forms of vasculitides presented with multisystem involvement. The overall mortality rate of 9% was attributed to active disease, sepsis, and complications of the primary disease.

ACKNOWLEDGEMENTS

We would like to thank Mr. Anil Sharma, Librarian, Patan Academy of Health Sciences, for his help during manuscript preparation.

REFERENCES

1. Watts RA, Scott DG. Recent developments in the classification and assessment of vasculitis. Best Pract Res Clin Rheumatol. 2009;23:429-43.
2. Watts R, Carruthers D, Scotts D. Epidemiology of systemic vasculitis: changing incidence or definition? Semin Arth Rheum. 1995;25;28-34.

3. Das RN, Paudel R. Spectrum of rheumatological disorders: an experience of 337 cases in a tertiary care hospital in Pokhara valley, Nepal. APLAR Journal of Rheumatology. 2006;9:248-56.
4. Paudyal B, Gyawalee M, Manandhar A, Sigdel K. Behcet's disease: an account of three cases. J Nepal Health Res Counc. 2012:10(22):250-53.
5. Paudyal BP, Pantha S, Ranjitkar N, Manandhar A, Arjyal A. A diagnosis missed for several years- Wegener's granulomatosis. Kathmandu Univ Med J. 2011;35(3):218-21.
6. Bloch DA, Michel BA, Hunder GG, McShane DJ, Arend WP, Calabrese LH, et al. The American College of Rheumatology 1990 criteria for the classification of vasculitis. Patients and methods. Arthritis Rheum. 1990;33:1068-73.
7. Jennette JC, Falk RJ, Andrassy K, Bacon PA, Churg J, Gross WL, et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum. 1994;37:187-92.
8. Mukhtyar C, Guillevin L, Cid MC, Dasgupta B, de Groot K, Gross W et al for the European Vasculitis Study Group. EULAR recommendations for the management of primary small and medium vessel vasculitis. Ann Rheum Dis. 2009;68:310–17.
9. Mukhtyar C, Guillevin L, Cid MC, Dasgupta B, de Groot K, Gross W et al for the European Vasculitis Study Group. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2009;68:318-23.
10. Agarwal I, Kumar TS, Ranjini K, Kirubakaran C, Danda D. Clinical Features and Outcome of Systemic Lupus Erythematosus. Indian Pediatr. 2009;46(17):711-15.
11. Watts RA. Epidemiology of Vasculitis in India- What is known? J Indian Rheumatol Assoc. 2005;13: 8-15.
12. Joshi VR, Mittal G. Vasculitis- Indian Perspective. J Assoc Physicians India. 2006;54Suppl:12-4.
13. Samant R, Vaidya SS, Nadkar MY, Borges NE. Spectrum of clinical features of vasculitides in a referral hospital from Western India. J Indian Rheumat Assoc.1997;5:6-14.
14. Sorensen SF, Slot O, Tvede N, Petersen J. A prospective study of vasculitis patients collected in a five year period: evaluation of the Chapel Hill nomenclature. Ann Rheum Dis. 2000;59:478-82.
15. Moriwaki R, Noda M, Yajima M, Sharma BK, Numano F. Clinical Manifestations of Takayasu Arteritis in India and Japan- New Classification of Angiographic Findings. Angiology The Journal of Vascular Diseases. 1997;48(5):369-79.
16. Jokar MH, Mirfeizi Z. Epidemiology of Vasculitides in Khorasan Province, Iran. Iran J Med Sci. 2015;40(4):362-66.
17. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013;65:1-11.
18. Sharma BK, Sagar S, Singh AP, Suri S. Takayasu Arteritis in India. Heart Vessels. 1992 (Suppl);7:37-43.
19. Chen M, Yu F, Zhao MH. Relapses in patients with antineutrophil cytoplasmic autoantibody-associated vasculitis: likely to begin with the same organ as initial onset. J Rheumatol. 2008;35(3):448-50.
20. Blanco R, Martinez-Taboada P, Rodriguez-Valverde V, Garcia-Fuentes M, Gonzalez-Gay MA. Henoch-Schonleinpurpura in adulthood and childhood: two different expressions of the same syndrome. Arthritis Rheum. 1997:40:859.