



# MoveS



Towards better pediatric rheumatology care.....

Bulletin of Pediatric Rheumatology Chapter, IAP

September, 2010

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Dear Colleagues and Esteemed Members of RCIAP;

Seasons Greetings and Welcome to the festive season!!

In this issue of MoveS we take you through an important aspect of Pediatric Rheumatology i.e. Vasculitis. Vasculitis constitutes a group of disorders that present with a variety of clinical features that pose difficulties in reaching a correct and timely diagnosis. More often than not there is a delay in diagnosis and institution of the appropriate treatment resulting in bad outcomes. An attempt is made in this issue of MoveS to give a simple and algorithmic approach to the diagnosis of Vasculitic disorders and a discussion on one of the most common vasculitic disorder seen in children. We hope that both the articles will be of benefit to the readers.

Any comments or suggestions on improvements are welcome.

Happy reading.

Dr. Rashna Dass, Shillong  
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# APPROACH TO A CASE WITH VASCULITIS

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## Abstract:

Vasculitis remains one of the most challenging groups of diseases both for diagnosis and therapy. The common pathology consists of inflammation of the blood vessels. As such there is an overlap of symptoms and signs in many cases. However some of the findings are specific to the vessel size involved and help in classify the vasculitic syndrome to a reasonable extent.

Key words: Vasculitis, approach, clinical

## Introduction:

Vasculitis means inflammation of the blood vessels. It forms one of the most challenging groups of disorders in terms of both diagnosis and treatment. The first case was described by Adolf Kussmaul and Rudolf Maier more than 150 years ago when they described a patient with what is today known as Polyarteritis nodosa (PAN) (1). Since then various forms and categories of the disease have been described.

## Basic pathology and pathogenesis:

The pathological changes common to all the vasculitic disorders is a destructive inflammation of the walls of the blood vessels resulting in either vessel wall occlusion or vessel injury, extravasation of red blood cells and aneurysm formation (Fig 1).

## Stratification of the childhood vasculitic syndromes:

Many classifications have been established over the years to try and stratify the childhood vasculitic syndromes. However many of these classifications were centered around adult age group and did not clearly help to differentiate various vasculitic disorders in children. The EULAR/PreS Consensus criteria for classification of childhood vasculitides published in 2006 (2) has tried to specifically define and stratify these disorders in children (Table 1).

**Table 1: Stratification of childhood vasculitic disorders:**

Type	Aorta and its branches	Predominantly medium sized vessels	Predominantly small sized vessels	Predominantly small sized vessels	Others
			Granulomatous	Non-granulomatous	
Takayasu arteritis	○				
Polyarteritis nodosa (PAN)		○			
Kawasaki disease		○			
Cutaneous PAN		○			
Wegeners granulomatosis			○		
Churg Strauss syndrome			○		
Microscopic polyangitis (PAN)				○	
Cutaneous leukocytoclastic vasculitis				○	
Urticarial vasculitis				○	
Behcets disease					○
Vasculitis associated with connective tissue disorders					○
Vasculitis associated with infection (hepatitis B), malignancy & drugs					○
Isolated vasculitis of Central nervous system					○
Cogan syndrome					○
Unclassified					○

**Clinical findings:**

Many of the symptoms and signs are common to this group of disorders and may overlap. Some of the common findings are as follows:

1. Systemic: Fever, weight loss, fatigue and arthralgias
2. Cutaneous findings: These may range from palpable purpura to urticaria, livedo reticularis, nodules and ulcers.
3. Organ specific involvement: This depends on the size of the vessel involved, degree of collateral circulation and the organ involved:
  - a. Neurologic: Mono or polyneuritis
  - b. Joints: Arthritis and effusions
  - c. Muscles: myalgia
  - d. Serous cavities: serositis
  - e. Cardiac: Hypertension, myocarditis, cardiomyopathy
  - f. Pulmonary: infiltrates or haemorrhage

Some of the typical findings which indicate the size of the vessel are indicated in Table 2 (3).

**Table 2: Typical clinical findings according to vessel involvement (3):**

Large vessel	Medium vessel	Small vessel
✓ Limb Claudication	✓ Cutaneous nodules	✓ Purpura
✓ Asymmetric B.P.	✓ Ulcers	✓ Vesiculobulbous nodules
✓ Absent pulses	✓ Livedo reticularis	✓ Urticaria
✓ Bruits	✓ Digital gangrene	✓ Glomerulonephritis
✓ Aortic dilation	✓ Mononeuritis multiplex	✓ Alveolar hemorrhage
	✓ Microaneurysms	✓ Cutaneous granulomas
		✓ Splinter hemorrhages
		✓ Uveitis/ Episcleritis / Scleritis

**Common laboratory findings:**

Some laboratory findings are found universally as a result of generalized inflammatory process such as raised erythrocyte sedimentation rates, C-reactive protein, leukocytosis, eosinophilia and haematuria.

**Algorithmic approach:**

In view of the overlap in clinical symptoms and signs as well as the laboratory findings it becomes difficult to exactly pinpoint the exact diagnosis of any patient with a vasculitic disorder. However an algorithmic and systematic approach helps to arrive at a reasonable clinical diagnosis (Fig 2).

**Mimics of vasculitis:**

Many other conditions can mimic vasculitis. Some of the common conditions are:

1. Atrial myxoma
2. Bacterial endocarditis
3. Infections such as pneumococcal and mycobacterial
4. Vasoconstrictive drugs such as ergot
5. Malignancy such as lymphomas
6. Connective tissue disorders
7. Thrombotic disorders such as anti-phospholipid antibody syndrome

These should be kept in mind while evaluating a case of suspected vasculitis. In developing countries such as India tuberculosis is a great mimic of this condition.

### Confirmation of diagnosis:

The clinical diagnosis is supplemented and confirmed by some specific laboratory tests such as tissue biopsy, X rays of the sinuses and chest, angiographic studies of the vessels, nerve conduction studies and assessment of auto-antibodies such as anti-nuclear antibody (ANA), anti-neutrophilic cytoplasmic antibody (ANCA). ANA would be positive in lupus associated vasculitis whereas cytoplasmic ANCA (c-ANCA) in Wegener's granulomatosis and perinuclear ANCA (p-ANCA) in microscopic polyangiitis. Rheumatoid factor positivity is seen in hepatitis B associated cryoglobulinemia.

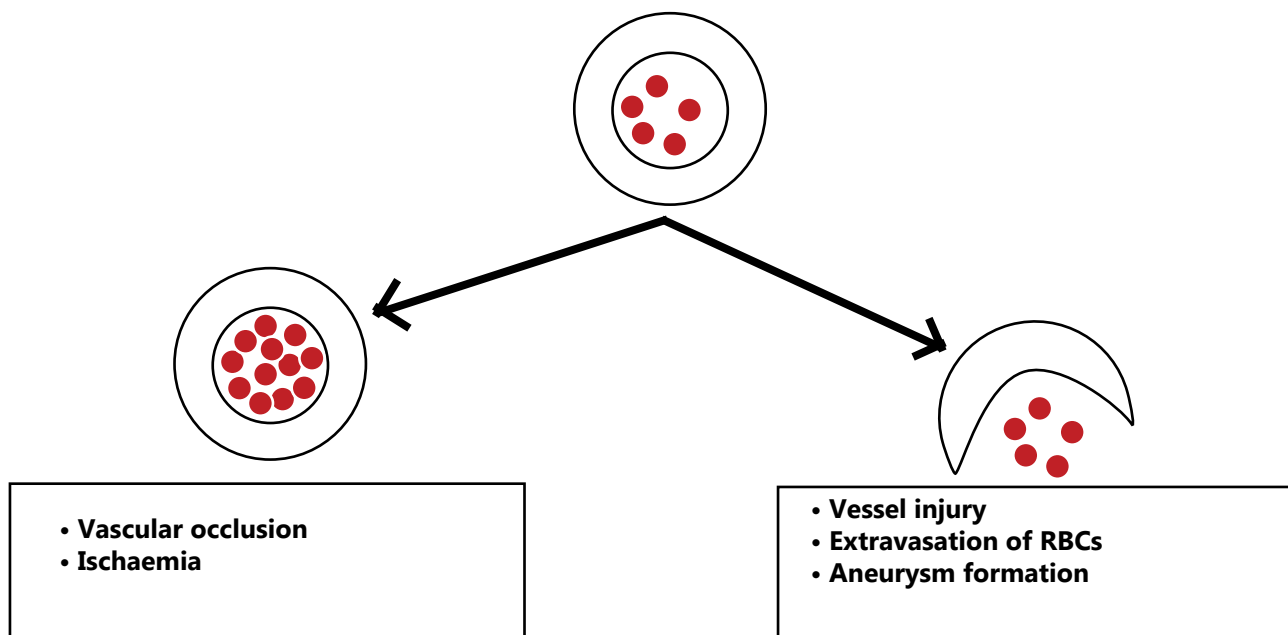
### Conclusion:

Vasculitides comprises of a diverse group of disorders resulting from a common pathology i.e. destructive inflammation of the blood vessels. These disorders have varied presentations but with common overlapping symptoms and signs. Diagnosis is aided by the fact that there are specific cutaneous and organ findings. Vasculitis should be considered whenever there is unexplained multisystem disease with evidence of vascular involvement. Other organs such as the eye, peripheral nervous system and the kidneys must be examined to pick up asymptomatic involvement. One must investigate for both symptomatic and asymptomatic involvement.

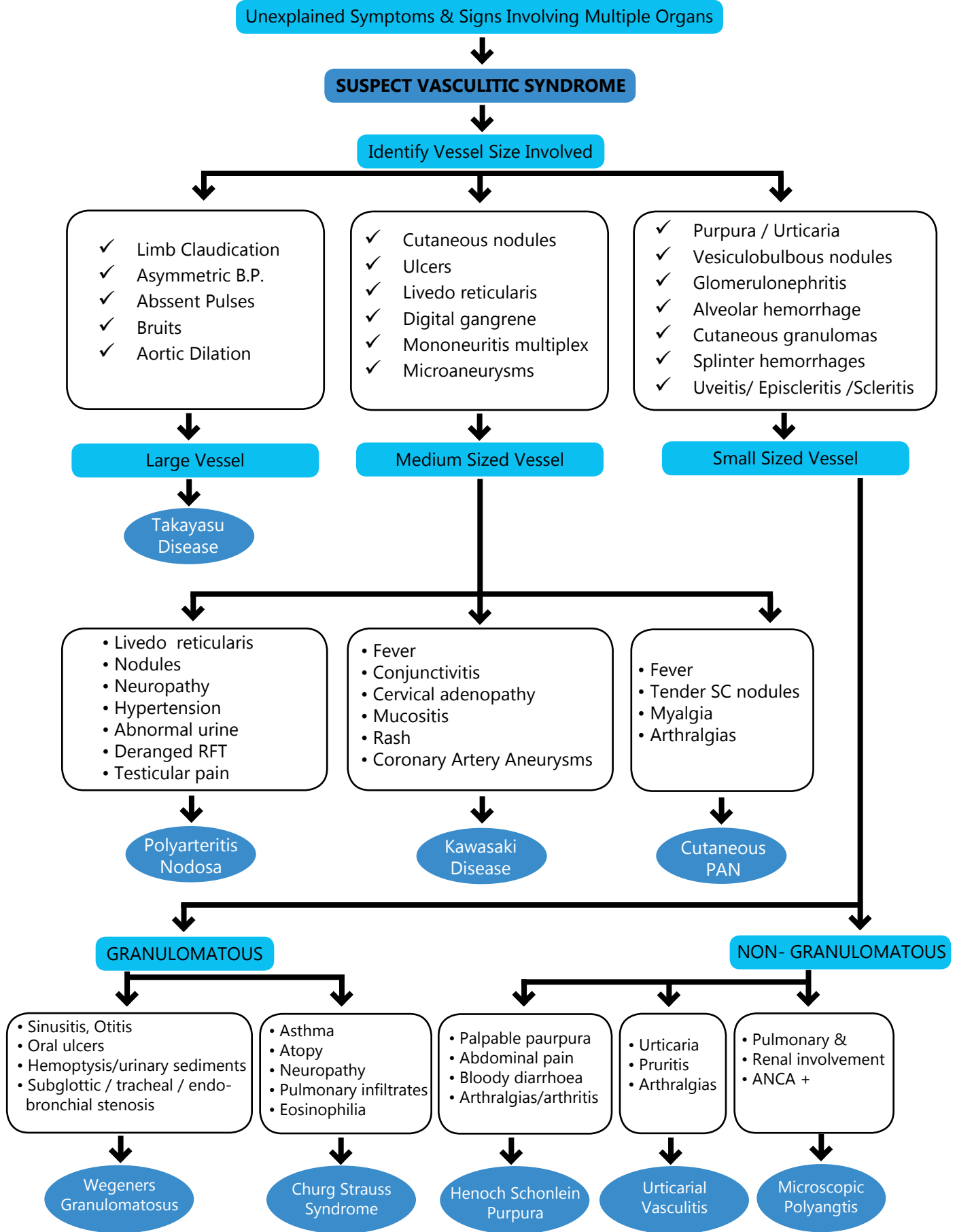
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**Fig 1: Common Pathology in Vasculitis**



**Fig 2: Algorithm for Diagnosis of a Vasculitic Disorder**



## Henoch Schonlein Purpura

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One of the most common vasculitides affecting children predominantly between 3-15 years of age. Rare in children less than 2 years of age. Characterised by non thrombocytopenic purpura, arthritis and arthralgia, abdominal pain, gastrointestinal haemorrhage and glomerulonephritis. Usually diagnosed early as the rash is the first to appear and the child is brought to medical attention.

### Etiopathogenesis:

Infections with  $\beta$  haemolytic streptococci has been implicated as a trigger. Recent vaccination and some viruses like varicella, rubella, rubeola, hepatitis A and B and Mycoplasma have also been implicated. Dietary allergens, dust and insect bites are also known to trigger the immune response as suggested by deposition of IgA.

### Clinical features:

Cutaneous involvement: Palpable purpura, most prominent on the lower extremity or on dependent, pressure bearing parts like thighs and buttocks. Lesions range from small petechiae to large ecchymosis and rarely hemorrhagic bullae may be seen. Occasionally few lesions may ulcerate. In a young child subcutaneous edema over the dorsum of hands and feet, around the eyes and over the scrotum may be seen.

### Gastrointestinal disease:

Abdominal pain is the most common presentation and usually occurs from a week of onset of rash to within a month. It is attributed to edema and sub mucosal haemorrhage leading to vasculitis of the bowel wall. It may lead to intussusception of the small bowel, gangrene or rarely perforation.

### Arthritis:

Arthritis or arthralgia of large joints like knees and ankles is common. Periarticular swelling with significant pain and limitation of movement is the usual presentation. Usually self limiting and abates without any residual abnormalities.

### Renal manifestations:

One third of children may have glomerulonephritis which occurs within a month of onset of rash. Renal manifestations include microscopic hematuria, proteinuria, nephritic syndrome, acute nephritic syndrome, hypertension or rarely renal failure. An increased risk of nephritis is associated with age of onset more than 7 years, persistent purpuric lesions, severe abdominal symptoms and decreased factor XIII activity. Initial 3 months are most critical in determining the extent of renal involvement and thus a careful monitoring of urinary sediment and renal function should

be done for at least 3 months from onset of rash.

Indication of renal biopsy is

- i. Acute nephritic syndrome or ARF
- ii. Nephrotic syndrome/nephrotic range proteinuria

**A referral to a nephrologist should be sought for in the following conditions:**

- i. Hypertension
- ii. Abnormal renal function
- iii. Macroscopic hematuria
- iv. Nephrotic syndrome
- v. Nephritic syndrome
- vi. Persistent proteinuria > 4 weeks

**Diagnosis: Classification criteria for Henoch-Schonlein purpura**

Palpable purpura (mandatory) in the presence of at least one of the following four features:

- Diffuse abdominal pain
- Arthritis (acute) or arthralgia
- Renal involvement (any haematuria and/or proteinuria)
- Any biopsy showing predominant IgA deposition

### Laboratory investigations:

No specific test is helpful to make the diagnosis, which usually remains clinical. Most investigations help to rule out other differentials and help to monitor the extent of organ involvement like the kidney.

Initial investigations should include Hemogram, clotting profile, renal function tests, liver function tests and urinalysis. In case of a diagnostic dilemma an autoimmune profile including ANA, ANCA, dsDNA, immunoglobulin profile, C3 and C4 should be done. Anaemia with leucocytosis with an elevated ESR is expected. Thrombocytosis may be present in some cases. Immunological profile is essentially normal.

In an unwell child, site of infection should be sought for with appropriate cultures of blood and urine or throat swabs and a chest X ray where indicated.

ASO titre and anti-DNAse B help in diagnosis of recent streptococcal sore throat and are helpful where renal disease might be complicated with post streptococcal glomerulonephritis.

### Course and Prognosis:

Usually self limiting within 4 weeks of onset. One third children might experience recurrences of rash and abdominal pain but each recurrence is briefer and milder than the prior one. Prognosis remains good for a majority of cases. A few children may have complications of the gastrointestinal tract in short term or nephritis in long term.

Major renal disease within first 3 months or numerous exacerbations with nephropathy constitute a poorer prognosis. Minimal change disease on renal biopsy has a favourable outcome in >75% children and recovery is expected within first two years. In contrast, >60% children with crescentic glomerulitis affecting >80% glomeruli progress to renal failure within one year of onset. Presence of nephritic or nephritic syndrome at onset is associated with worst outcome.

#### Differential Diagnosis:

A typical presentations may mimic small vessel vasculitides like microscopic polyarteritis, Wegener's granulomatosis, isolated leucocytoclastic vasculitis and SLE. Thrombocytopenic purpura and septicaemia are other differentials which should be considered.

Acute hemorrhagic edema of infancy is sometimes considered as a variant of HSP. It presents with large purpuric lesions with central clearing along with edema mainly affecting face, auricles and extremities. It rarely involves other organs and few have IgA deposition.

#### Treatment:

Mainly symptomatic. Arthritis and arthralgia are managed with rest and NSAIDs. Corticosteroids do not have a role in preventing complications like abdominal pain and renal complications. Hypertensive therapy might be required in the presence of hypertension.

Systemic corticosteroids are indicated in the presence of severe gastrointestinal hemorrhage, here oral prednisolone 1-2mg/kg can be given for a week and tapered over next two to three weeks.

In presence of moderately severe to severe renal disease glucocorticosteroids are indicated. Prednisolone with cytotoxic agents like Azathioprine are associated with a better outcome. Therapy with drugs like cyclosporine A, Cyclophosphamide and IVIG has been reported to be successful. Plasma exchange has also been used in severe HSP nephritis.



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